

OBSTETRICAL AND GYNECOLOGICAL SURVEY

Volume 4

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THE WILLIAMS & WILKINS COMPANY

BALTIMORE, MARYLAND

Review

THE DIAGNOSTIC USE OF THE BASAL BODY TEMPERATURE IN GYNECOLOGY AND OBSTETRICS

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HISTORICAL BACKGROUND AND REVIEW OF THE LITERATURE

As far back as 1838 von Fricke studied the temperature of the axilla, vagina and uterus in relation to menstruation. His series consisted of 24 patients and his observations were made 8 days and 4 days before menstruation, during menstruation and in pregnancy and the puerperium. He concluded that the vagina had a higher temperature than either the axilla or the uterus and that menstruation and pregnancy had no influence on the temperature. However, he did not make daily observations throughout the menstrual cycle. There is no indication in von Fricke's report that the temperatures of the various regions of the body measured were obtained under basal conditions.

About 30 years later, Squire (1868) reported on "Puerperal Temperatures" to the Obstetrical Society of London. In his paper he referred to his observations of the basal body temperature in relation to events of the menstrual cycle. He observed that the temperature during pregnancy was relatively high and did not oscillate, whereas, at the time of menstruation there was a considerable fall in temperature and a variable rise shortly before. He further reported a fall in the temperature after childbirth and a rise when lactation began. Thus the cyclical nature of the basal body temperature in women was probably first recorded about 80 years ago. At that time the cyclical wave-like variation in the basal body temperature was correlated with the various events of the menstrual cycle and was not in accord with the earlier observations of von Fricke.

More detailed investigations of the basal body temperature and its relationship to menstruation were carried out subsequently by Rabuteau (1870), Jacobi (1876), Goodman (1878), Stephenson (1882), Reim (1884), von Ott (1890), Giles (1897) and Mandl and Bürger (1904). In addition to cyclical variations in the basal body temperature, wave-like fluctuations of many other physiological mechanisms of the human female were observed by these authors. These included changes in volume of urine excreted, carbonic acid excretion, oxygenation power of the blood, urea excretion, arterial tension, pulse rate, muscular strength and nervous reflexes.

It remained for van de Velde (1904 and 1930) to point out the relationship between the wave-like fluctuations of the basal body temperature and ovulation. He observed the temperature changes of one woman throughout the duration of pregnancy. Immediately after the onset of pregnancy, the exact date of which was known, the temperature rose rapidly and remained at a high

level with no further cyclical fluctuations. During the last 2 months the temperature gradually fell and began to assume a form suggestive of the cyclical fluctuations of the nonpregnant state.

Oster (1910) and Flaskamp (1928) reported further on the ovulatory rise of the basal body temperature.

Upon examining the data presented in van de Velde's monograph, Harvey and Crockett (1932) were of the opinion that the author had demonstrated: "(1) under normal circumstances the cycle is regular in its wave-like fluctuations; (2) with the menopause it ceases to appear, the curve becomes irregular and lacks its former marked excursion; (3) that under certain abnormal physiological conditions the cyclical fluctuations fail to appear; but (4) that their reappearance can be artificially induced by 'ovarian tablet' therapy; (5) the ovarian cycle is presumably related to the menstrual cycle but (6) menstruation is not a necessary concomitant of ovulation (or rather, more precisely, of the temperature cycle)." These authors observed the morning oral temperatures of a 26 year old woman daily for 13 consecutive menstrual cycles and found that rhythmic wave-like fluctuations occurred coincidentally with the events of each cycle. They constructed a composite curve by fusing the observed temperatures for the 13 cycles and in this manner determined that the cyclical fluctuations were real as well as apparent.

Men, children, and women past the menopause do not exhibit cyclical fluctuations of the basal body temperature (Kleitman and Doktorsky, 1933, Kleitman et al. 1933, and Vollmann, 1940). The latter also observed that during the amenorrhea associated with lactation, there were no cyclical variations. Just before the onset of the first menses after delivery, however, the temperature again was found to be diphasic in character. The same author made use of temperature curves to determine the lengths of the postmenstrual and premenstrual phases of the cycle. He observed that the duration of the premenstrual phase was relatively independent of the length of the menstrual cycle, whereas the postmenstrual phase varied directly with the length of the menstrual cycle.

Seward and Seward (1936) reviewed the various factors affecting menstruation and the menstrual cycle of women. They added no new data in regard to the basal body temperature.

Rubenstein and Lindsley (1937) demonstrated a statistically significant correlation between the fluctuations of the basal temperatures and vaginal smears in 5 menstrual cycles observed in 4 young adult women without pelvic abnormality. Rubenstein (1937) observed a constant relationship between the lowest body temperatures of the month and the characteristic ovulation smear, and between the highest body temperatures and the characteristic premenstrual smear. He concluded that the temperature cycle was as trustworthy an indicator of ovarian function as the vaginal smear. Rubenstein (1939) made use of the basal body temperature curve for the detection of ovulation in the investigation of sterility.

Zuck (1938) in reporting basal body temperature studies for the detection of

ovulation published the temperature curves recorded during the last menstrual cycle and onset of pregnancy in 20 women. He observed that the temperature during pregnancy remained high as in the last part of the menstrual cycle and that the prolonged elevation of the temperature could be used as a sign of pregnancy before other methods of diagnosis were positive. He reported his observation that ovulation as well as menstruation may occur after conception begins. His diagnosis of early pregnancy in the case in point was apparently made on the basis of breast tenderness and subsequent delivery date of fetus—since the basal body temperature curve in the patient observed fluctuated normally for a complete cycle after the diagnosis of pregnancy was made.

Raoul Palmer, following the appearance of a paper by Mocquot and Moricard (1938) on the presence of glycogen in the endometrium as a test for the effect of progesterone, pointed out that in all cases in which biopsies of the endometrium were performed before and after the "thermal shift" of the mid-intermenstrual portion of the basal body temperature curve of normally menstruating women, those specimens obtained before the shift contained no glycogen, while those obtained after the shift showed glycogen to be present.

Palmer and Devillers (1939) studied the basal body temperatures in 75 women with gynecological complaints. From their series of abnormal individuals they were not able definitely to fix the date of ovulation by the temperature changes alone. They did conclude, however, that the period of maximum fecundity corresponded with the time of minimal temperature. They associated symptoms of ovulation (pain, hemorrhage, leucorrhea, mastalgia, etc.) with this period in the cycle. They were able to foretell quite accurately the date of subsequent menstruation in women with irregular menses and thereby avoided doing repeated endometrial biopsies in order to obtain real premenstrual specimens. Palmer and Devillers (1939) checked the thermal effects of sex hormones in women and observed that in ovariectomized women who ran a nonfluctuating basal body temperature curve, the injection of 5 milligrams of estradiol benzoate produced a decrease in temperature lasting several days, and that the injection of 10 milligrams of progesterone produced an increase in basal body temperature for two days. The injection of 10 milligrams of testosterone propionate produced a transient drop in temperature.

Rubenstein (1940) favored the combined use of basal body temperatures and vaginal smears as a technic for the study of functional sterility, and claimed accuracy in detecting early pregnancy as great as with the use of the Friedman pregnancy test. The diagnosis of early pregnancy by temperature curves in 8 patients unaware of the existence of pregnancy because of menstrual flow was confirmed by the recovery of fetal membranes.

Since 1940 a great many authors have adopted the use of the basal body temperature method in their investigation of infertility problems. Barton (1940) reviewed the subject and presented an excellent review of the literature. Greulich (1946) performed laparotomies on 14 patients in order to correlate findings at the time of operation with changes in the basal body temperature record. Eight of his patients whose basal body temperature indicated ovulation ex-

hibited compatible evidence in their ovaries, and 5 whose temperatures indicated the absence of ovulation, exhibited no evidence of ovulation on the surface of their ovaries. The basal body temperature record of 1 patient indicated that ovulation had occurred, but no such evidence was found in either ovary. This is a very important observation in view of further discussion given below.

Palmer (1942) reviewed the subject of basal body temperatures in women and presented his findings with reference to various menstrual disorders. The basal body temperature record was used to demonstrate that the normal variation in the length of the menstrual cycle varied with the length of the pre-ovulatory phase. An absolute correlation between the high temperature phase of the cycle and the presence of secretory endometrium was demonstrated. The inhibition of ovulation resulting from estrogenic hormone therapy in the early part of a normal menstrual cycle also was demonstrated by use of the temperature curve. Menstrual disorders were investigated more satisfactorily by the use of basal body temperature records than by hormone excretion determinations, endometrial biopsies and vaginal smear examinations.

Martin (1943) confirmed earlier work on the correlation between the premenstrual rise in the basal body temperature and secretory changes in the endometrium.

Lyon (1943) demonstrated the relationship between primary dysmenorrhea and ovulation and later (1946) the incidence of ovulation during the puerperium by use of the basal body temperature curve.

Tompkins (1945) introduced a standardized graph for use in detection of ovulation for purposes of planned pregnancies and for a method of contraception.

Nieburgs (1945) presented an excellent review of the subject. He confirmed earlier work on the thermal effects of the various steroid hormones. He supported the work of the Biskinds (1944) that inactivation of estrogen may be revealed by the effect of Vitamin B in elevating the basal temperature in a patient with protracted follicular activity. He concluded that dysmenorrhea is the result of a quantitative disparity between estrogen and progesterone withdrawal in the menstrual cycle.

Barton (1945) in addition to reviewing the subject, presented a case of secondary amenorrhea with a diphasic basal body temperature curve. She suggested that the "rate of thermal shift" may be important in actually detecting ovulation and that possibly a thermal shift of an abnormal type may occur with the clinical signs of ovulation but in the absence of the mechanism thereof. She stated "The thermal shift may be an indicator of but not positive evidence of ovulation." This is an extremely important point in view of discussion to be given below on the possibility of the occurrence of all the signs and symptoms of ovulation in the absence of the actual mechanical rupture of the ripened Graafian follicle, extrusion of the ovum and spilling of follicular fluid in the peritoneal cavity.

The following authors have contributed confirmatory evidence for the most part to observations and statements made above:

Vollman (1940); Williams and Simmons (1942); Williams (1943); Salerno (1943); Greulich (1943); D'Amour (1943); Viergiver and Pommerenke (1944 and 1946); Kleitman (1944); Halbrecht (1945); Grenville-Mathers (1945); Davis (1946); Tyler and Payne (1947); Buxton and Atkinson (1948); Davis and Fugo (1948); Kleitman and Ramsaroop (1948).

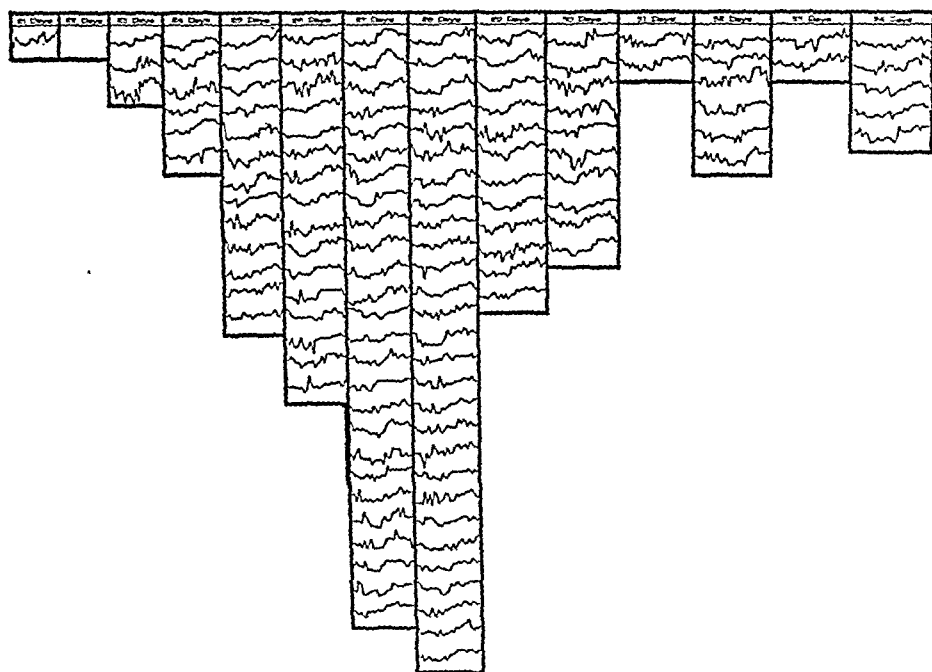


FIG. 1. Basal body temperature curves recorded by 35 normal women during 130 complete menstrual cycles. The curves are grouped according to the lengths of the cycles and show a normal distribution of 21 to 35 day cycles. Although there are rather marked variations in temperature from day to day every curve exhibits a diphasic tendency.

DISCUSSION

Thus it has been established that the basal body temperature of regularly menstruating women fluctuates cyclically and that its rises and falls actually result from the action of the two types of hormones (estrogen and progestogen) elaborated by the ovary. In Figure 1 are charted the individual basal body temperature curves of 35 normally menstruating women recorded during 130 complete menstrual cycles. The curves have been grouped according to the length of the cycles, the latter showing the accepted normal variation. Although there are occasionally wide variations in an individual's temperature, every curve in the chart is diphasic. During the estrin phase of ovarian activity the temperature is relatively low and during the progestin phase it is relatively high. There is a fall in temperature associated with the onset of menstruation followed by a rise in temperature at approximately the midin-

termenstruum. The rising temperature section of the curve which normally occurs at midintermenstruum is called the "thermal shift."

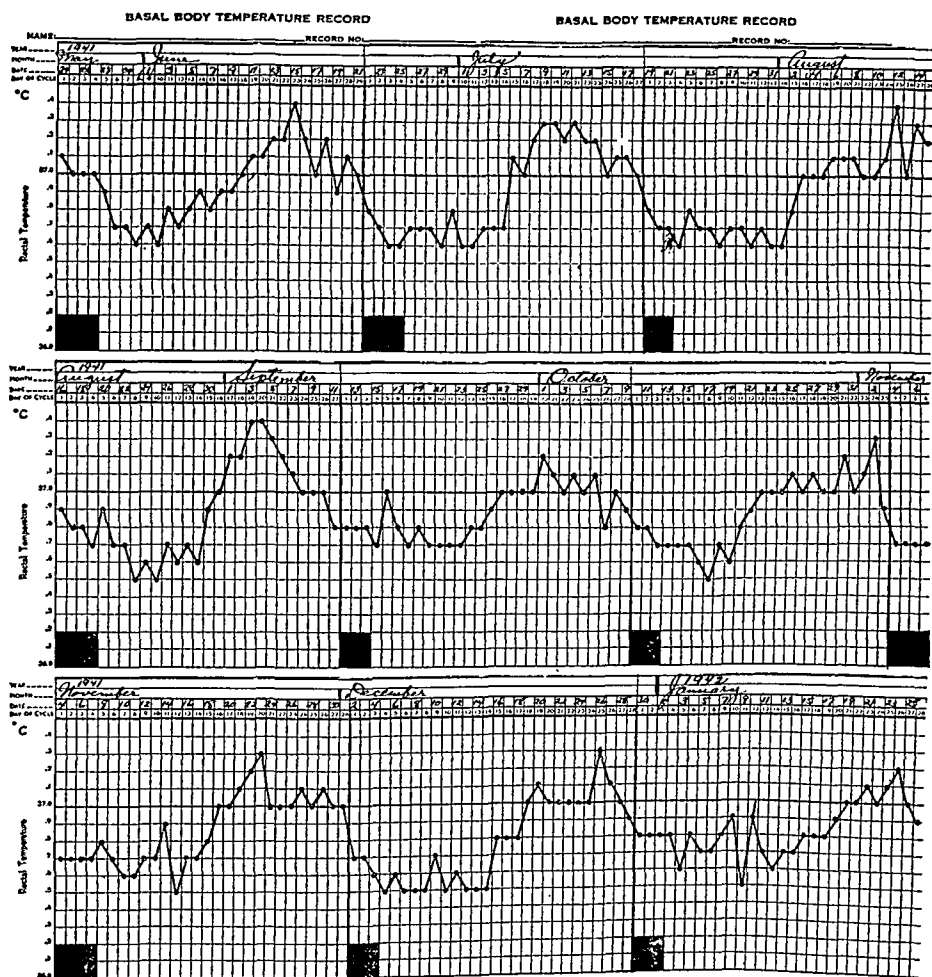


FIG. 2. Typical example of normally occurring menstrual cycles and normal basal body temperature curve during 9 successive cycles in the same individual. Note the regularly occurring diphasic character of the curve. Temperature fall and low level are associated with the onset of menstruation, the pre-ovulatory phase of the ovarian cycle, and the proliferative phase of the endometrial cycle. The thermal shift and high level are associated with ovulation, the post-ovulatory phase of the ovarian cycle and the secretory phase of the endometrial cycle.

Figure 2 is a typical record of the basal body temperature of one individual recorded for 9 consecutive normal menstrual cycles. Wide variations in the temperature from day to day are not so obvious when the record is carefully kept for long periods of time by the same individual. No real exceptions to the

correlation between the relatively high temperature phase of the menstrual cycle and secretory endometrium have been observed.

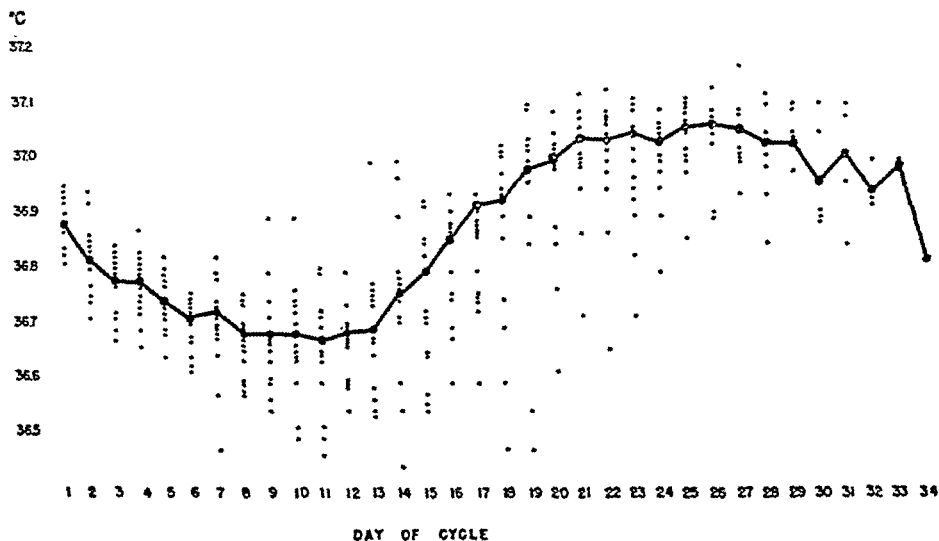


FIG. 3a. Composite curve constructed from all the curves in Figure 1 and superimposed so that the *first* day of each cycle coincides. Note the poor fitting of superimposed curves in the broad area covered by thermal shift or rising temperature section of the curves.

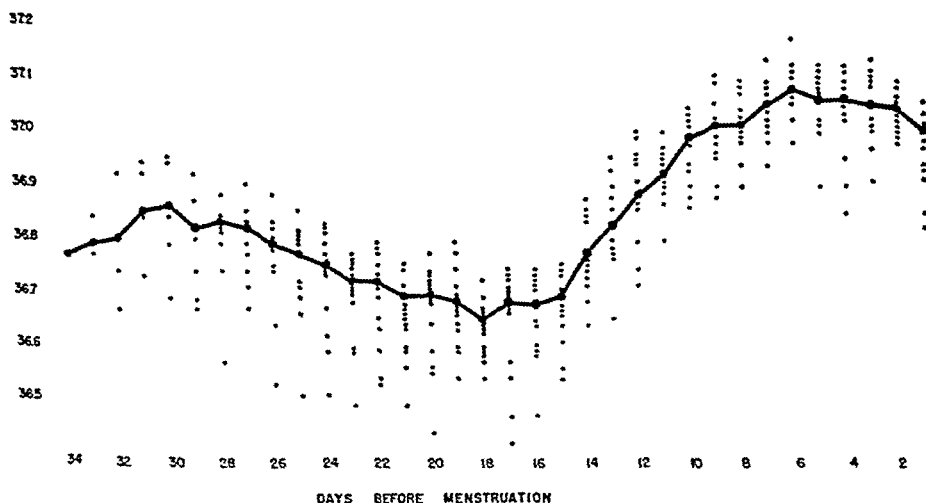


FIG. 3b. Same as Figure 3a except that the curves are superimposed with the last day of each cycle coinciding regardless of the cycle length. Here there is good fitting of the rising temperature section of the curves.

Figure 3 demonstrates the uniformity in length of the post-ovulatory or premenstrual phase of the menstrual cycle. Figure 3a shows the poor fitting of

the temperature rise which results when curves obtained from patients with menstrual cycles of varying length are superimposed with the *first* day of each cycle coinciding. Figure 3b demonstrates better fitting of the same curves when they are superimposed with the *last* day of each cycle coinciding. Lining up the curves in this manner is justified by the following observation—and serves to confirm the finding reported by others—that the duration of the progestin phase of ovarian activity is relatively constant and independent of the length of the menstrual cycle. The same relative uniformity in the length of the high temperature phase has been observed in longer menstrual cycles (45 to 162 days)

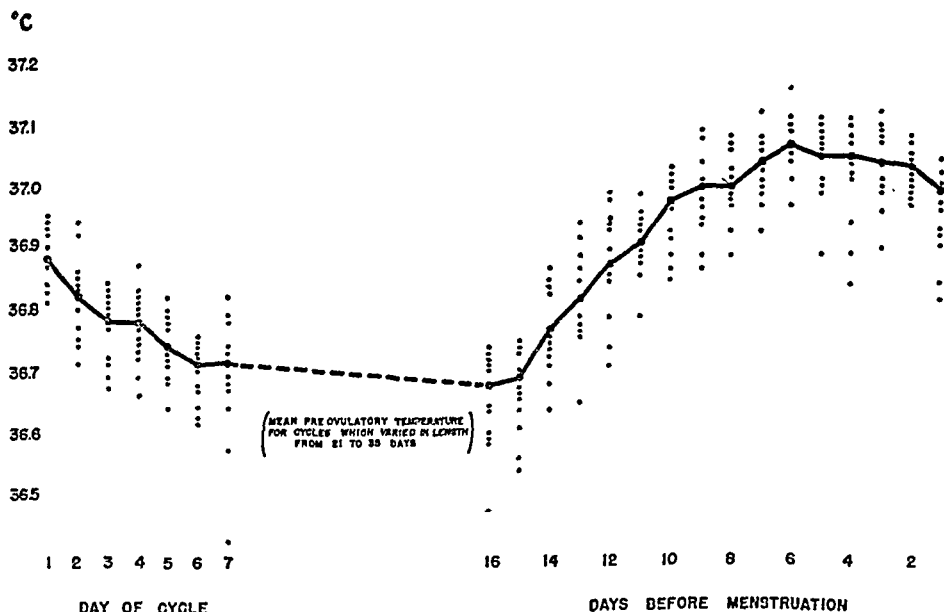


FIG. 3c. All the curves in Figure 1 have been divided between the 17th and 16th day before the next menstruation and the divided parts superimposed so that the first and last days of each cycle coincide. There is good fitting of both the "menstrual fall" and the "ovulatory rise" in this composite curve.

and confirmed by the finding of secretory endometrium obtained during the phase of elevated temperature and proliferative endometrium in specimens taken before the "thermal shift."

Good fitting of both the "menstrual fall" and the "ovulatory rise" of several basal body temperature curves is obtained when the latter are first divided at about 16 days before the end of the cycle. Thus, Figure 3c shows the best fitting of both phases of the temperature curve when the first and last days of each cycle coincide.

Standardized forms on which a patient may record her basal body temperature in a uniform manner such as those introduced by Hamblen (1945) and Tompkins (1945) are of great value. Unless one cares to have many types of

forms and graphs, it is advisable to standardize on one form or another. Since it is likely that the basal body temperature record will be useful in many gynecological disorders other than infertility, it is probably desirable that forms bearing instructions to the patient should not appear to be intended exclusively for infertility problems. Suggested form sheets* are shown in Figure 4 for the Fahrenheit and Centigrade temperature scales. The most satisfactory form is one in which the unit of measurement in the vertical direction for the temperature scale is equal to the unit of measurement in the horizontal direction for the day of the menstrual cycle when the Fahrenheit scale is used (i.e., one-tenth of a degree F. and one day of the cycle). The vertical unit should be correspondingly increased for each tenth of a degree when the Centigrade temperature scale is used. The magnification of the magnitude of rise and fall of temperature is optimal when these specifications are followed. Standardization in this manner also makes temperature curves more readily comparable when Fahrenheit and Centigrade temperature curves are compared clinically.

Instructions to the patient in the manner of recording her basal body temperature are most easily given in the form of a detailed explanation, instructions and a sample temperature record printed on the reverse side of the standardized graph, as in Figure 5. A diagram of a thermometer with its scale extended to the corresponding horizontal lines on the temperature graph is an excellent aid to patients.

Vaginal, rectal, axillary and oral basal body temperatures have been used, and each shows comparable cyclical fluctuations. The rectal temperature has the greatest number of advocates and is probably the most practicable. Oral temperatures may tend to be false when recorded by patients who have a tendency to doze with the mouth partially open during the 5 minutes or more of rest in the early waking hours of the morning when the temperature is being measured. In the case of a young girl in whom the vaginal temperature was being recorded for the investigation of a menstrual disorder, the patient inadvertently inserted the thermometer into the urethra and, moving about with the thermometer in place, broke it so that it was necessary to remove the broken pieces through a cystoscope. A similar accident, of course, could happen when the temperature is taken per rectum, but the problem of removing a broken part probably would not be so great.

The importance of recording the temperature under basal conditions and preferably at the same time each morning should be stressed. Figure 6a is the basal body temperature record of a normal woman who was hospitalized at complete bed rest from the 12th to the 18th day of her cycle for the sole purpose of recording her temperature. Figure 6b is the horizontally extended 12th to 18th day section of the temperature curve in Figure 6a showing the observed temperature at hourly intervals. The first temperature each morning was taken at 6:00 a.m. after a good night's sleep. Subsequent temperatures at hourly intervals until 10:00 p.m. were taken during continuous complete bed

* Supplied by the Witmer Record Company, Kansas City, Mo.

BASAL BODY TEMPERATURE RECORD

NAME: _____ RECORD NO: _____

YEAR: _____
 MONTH: _____
 DATE: _____
 DAY OF CYCLE: _____

°C

Rectal Temperature

37.0
.9
.8
.7
.6
.5
.4
.3
.2
.1
36.0

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40

YEAR: _____
 MONTH: _____
 DATE: _____
 DAY OF CYCLE: _____

°C

Rectal Temperature

37.0
.9
.8
.7
.6
.5
.4
.3
.2
.1
36.0

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40

FIG. 4a. Basal body temperature graph for centigrade scale

rest. Thus all temperatures were recorded under conditions which might be regarded as basal as far as the determination of one's basal metabolic rate is

BASAL BODY TEMPERATURE RECORD

NAME: _____ RECORD NO: _____

YEAR _____

MONTH _____

DATE _____

DAY OF CYCLE

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
<div> $^{\circ}\text{F}$.8 .7 .6 .5 .4 .3 .2 .1 99.0 .9 .8 .7 .6 .5 .4 .3 .2 .1 98.0 .9 .8 .7 .6 .5 .4 .3 .2 .1 97.0 </div>																																							

Rectal Temperature

YEAR _____

MONTH _____

DATE _____

DAY OF CYCLE

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
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Rectal Temperature

FIG. 4b. Basal body temperature graph for Fahrenheit scale

concerned. Nevertheless, the lowest temperature each day always was observed at the earliest time taken, i.e. 6:00 a.m. Temperatures taken during

BASAL BODY TEMPERATURE

The function of the ovaries is reflected in one's basal body temperature (BBT). Your doctor has requested that you record your BBT daily for a period of time so that he may evaluate the function of your ovaries in conjunction with various other procedures which are required for a thorough investigation of your problem. The BBT is most accurately determined when taken rectally at the same time every morning just prior to rising. Variations in the BBT are very slight so that it is essential that the following instructions be followed with utmost care.

INSTRUCTIONS

1. Obtain a Basal Temperature Thermometer with Centigrade scale.
2. Shake the thermometer down at night before retiring and place it on a bedside table. (It may be most practical to stand it in a small suitable container of lubricant.)
3. Upon awakening in the morning, before stirring from the bed, insert the rectal thermometer and rest with it in place for five minutes. Record the temperature reading for the appropriate date on the chart on the reverse side of this page as a black dot.
4. If the night before has been a restless one or if you have a headache or a cold, the temperature may not be a strictly "basal" one and the recorded dot should be transformed into an asterisk to indicate this variation. (See sample chart below.)
5. Record the occurrence of menstrual flow whether it be normal or abnormal as shown on the sample chart.
6. The BBT should be recorded throughout the period of menstrual flow and usually for two or more complete menstrual cycles.
7. Temperature must be taken at the same time every morning preferably at 6 or 7 A.M.

SAMPLE CHART

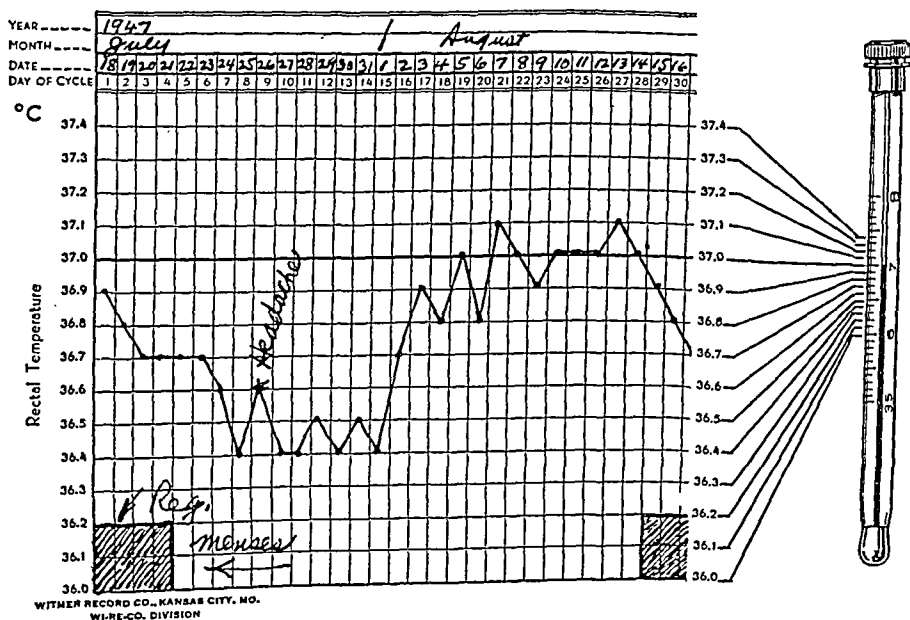


FIG. 5. The explanation, instructions to the patient and sample temperature record for use by the patient and her physician printed on the reverse side of the basal body temperature graph in Figure 4.

the pre-ovulatory or post-ovulatory phase, when normally there are no marked variations from day to day, by an individual who records her waking temperature at 6:00 a.m. on one day and upon waking as late as 11:00 a.m. the next day,

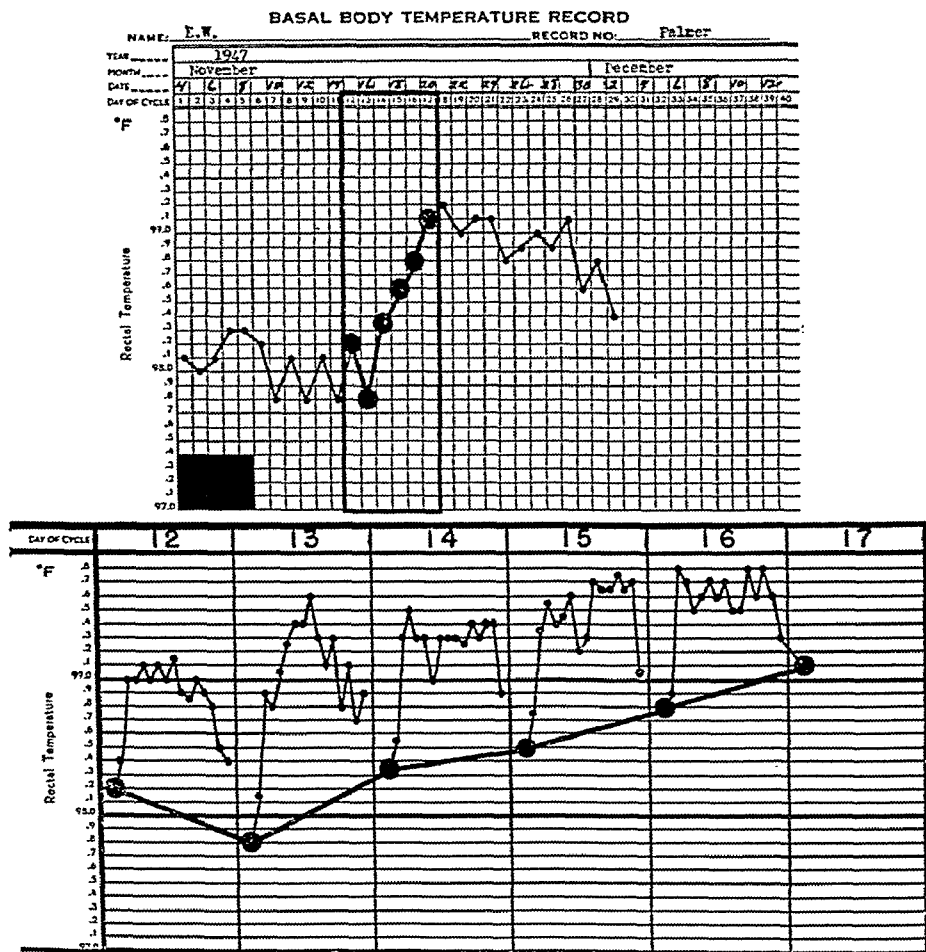


FIG. 6a. Normal basal body temperature curve of a patient during one complete cycle with the temperatures during the thermal shift accentuated.

Fig. 6b. Horizontally extended twelfth to eighteenth day section of the basal body temperature curve in Fig. 6a to show the variation following the 6 a.m. temperature when taken at hourly intervals until 10 p.m. each day. Note that the temperatures taken after 6 a.m. even though recorded under conditions regarded as basal, show rises during each day which are as high as the "ovulatory rise" of the 6 a.m. temperature.

will show a rather marked relative rise on the day when the waking hour was 5 hours later than usual. Strict adherence to the instructions for taking the temperature at a regular time according to a regular plan is necessary in order to obtain a smoothed-out basal body temperature curve similar to the "Bloxham"

curves reported by van de Velde (1904). Bloxham's method was to record the average of 4 temperatures taken at 4-hour intervals each day a patient was under observation. However, the increased frequency of taking the temperature and smoothing out a temperature curve by Bloxham's method is unnecessarily troublesome and gives no better curves than those recorded from single daily temperatures taken uniformly at the same time each morning.

INTERPRETATION OF BASAL BODY TEMPERATURE CURVES

Ovulation: The time of ovulation may be determined from the basal body temperature record more easily than by any other means. However, it may be stated again, as noted by Barton and Wiesner (1945) that "The thermal shift may be an indicator but not positive evidence of ovulation." In view of our knowledge that some laboratory animals frequently have corpora lutea which function endocrinologically but in which an ovum may be imprisoned, and the observation reported by Greulich (1946) that a patient's basal body temperature record showed a thermal shift but her ovaries exhibited no evidence of follicle rupture, it is possible that all the signs, symptoms and endocrine function of a corpus luteum may occur without the ovum actually having been mechanically extruded from a mature ruptured Graafian follicle. Greenblatt and Krafka (1941) demonstrated a ripened follicle apparently ruptured but with an ovum still in situ. The many cases of infertility which are observed in married couples in whom no pathology may be found lead us further to conclude that the physiology of a corpus luteum may appear to be normal and all the endocrinological changes in the human female due to a functioning corpus luteum may occur but, actually, mechanical rupture of the ripened follicle may not have occurred. There is still need for a method to detect rupture of a mature Graafian follicle and the mechanism of ovulation as such. The thermal shift of the basal body temperature and the secretory changes in the endometrium should be regarded as being due only to the luteinization of a mature Graafian follicle, with or without rupture of that follicle, rather than to real ovulation and the luteinization which follows follicle rupture.

When ovulation has occurred the basal body temperature is of the greatest value in detecting its time of occurrence. Even then, however, one cannot always determine the one day of optimum fertility as far as ovulation is concerned. At best one can only state that if ovulation has occurred the time of optimum fertility is the 2 to 5 day period which spans the rising temperature phase or thermal shift of the basal body temperature.

Palmer (1948) has suggested that infertility due to the mechanical failure of ovulation may be characterized by a basal body temperature curve in which 3 to 5 days are required for the temperature to rise to a level significantly above the low temperature phase. He has shown that real ovulation may be characterized by a temperature curve in which the ovulatory rise is significantly abrupt in 24 hours.

The basal body temperature curves shown in Figure 3 have been regarded as being characteristic of normal ovarian function. However, if by 'normal'

one means ovarian function associated with real mechanical ovulation, a temperature curve characteristic of follicle rupture may be quite different from those shown in Figure 3. Normal endocrinological ovarian function may not always be associated with the follicle rupture phenomenon. Thus the basal body temperature curve characteristic of follicle rupture or fertility is shown in Figure 7. This curve is a composite one constructed by superimposing individual curves recorded by 22 women during ovarian cycles in which conception was known to occur. Here the thermal shift is abrupt, the rise being significant in a period of 24 hours. The mean daily temperatures used to construct the curve in Figure 7 were calculated from all the temperatures recorded after the individual curves were arranged and superimposed with the day during which the temperature began to rise, coinciding.

°C

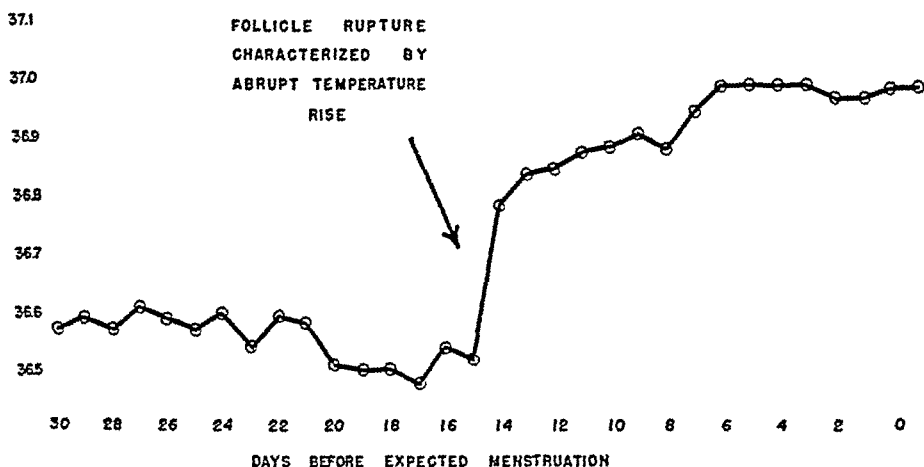


FIG. 7. Composite curve constructed from the individual curves recorded by 22 women during ovarian cycles in which conception occurred. The curves were superimposed so that the day during which the ovulatory rise of the temperature began, coincides. (The duration of the pre-ovulatory phase in these 22 cycles ranged from 9 to 29 days, average 17.3 days.)

The duration of the pre-ovulatory phases of the fertile cycles of the 22 women ranged from 9 to 29 days. This explains why a certain day of the menstrual cycle, without reference to the basal body temperature curve, cannot be depended upon to identify the time when ovulation occurs with respect to the previous menses. It is assumed that rupture of the follicle occurs about 14 days prior to menstruation and that, had conception not occurred in these 22 women, they would have experienced menstrual cycles of 23 to 43 days in length.

Menstruation: In normally menstruating women the basal body temperature falls significantly on the morning of the day during which the menstrual discharge first appears. Slight irregularities of this relationship may not be important or apparent either to a patient or to her physician. Extreme variations, however, are significant.

Shortened post-ovulatory phase: It has been shown that the length of the normal menstrual cycle varies directly with the length of the pre-ovulatory phase of the cycle. Thus a patient having 21 day cycles normally would exhibit a 7 day pre-ovulatory phase and a 14 day post-ovulatory phase of her cycle. A patient having 35 to 40 day cycles normally would exhibit a 21 to 26 day pre-ovulatory phase and a 14 day post-ovulatory phase. Occasionally, however, a patient may exhibit a post-ovulatory phase significantly less than the average of 14 days (See Figure 8a). When this phase is as short as 7 or 8 days and the patient presents an infertility problem it is possible that the infertility may be due to premature degeneration of the corpus luteum. This would account for the shortened post-ovulatory temperature phase with menstruation occurring before the normal time of implantation of a fertilized ovum. If this can be demonstrated to be the cause for some cases of infertility, efforts at treatment should be directed toward prolonging the life of the corpus luteum and thereby the duration of the post-ovulatory phase to its normal duration (See Figure 8b).

Premature bleeding: Occasionally a patient with menometrorrhagia may exhibit a basal body temperature curve which is normal but which is associated with prolonged or irregular phases of bleeding (See Figure 9). Bleeding may occur at any time, but usually at about the time of the thermal shift and may continue irregularly for 10, 12 or 14 days, or until after the subsequent menstrual fall of the temperature. Endometrium obtained from such patients during the high temperature phase usually reveals the so-called "mixed pattern" and results in the clinical diagnosis of "incomplete shedding" of the endometrium. Actually the bleeding which occurs is not synchronized with the menstrual fall of the basal body temperature and might be regarded as premature bleeding, possibly due to some defect in the endometrium. Instead of regarding the onset of such bleeding as being the beginning of a menstrual cycle with incomplete shedding of the endometrium, one might more correctly interpret these findings as premature bleeding. The endometrium is not due to shed itself completely until after an average of 14 days of corpus luteum activity and the time of the menstrual fall of the basal body temperature. The normal bleeding and shedding probably is that which continues to occur after the fall of the basal body temperature. The several days of bleeding before the fall of the basal body temperature are actually the last days of the previous menstrual cycle and are not associated with the normal degeneration of the corpus luteum for that particular cycle.

Pregnanediol has been found in the urine during bleeding when the basal body temperature is in the post-ovulatory phase. Pregnanediol is not demonstrable in the urine, however, during normal menstruation, that is, after the menstrual fall of the basal body temperature.

Pregnancy: The post-ovulatory phase of the basal body temperature normally is sustained for an average of 14 days. When the post-ovulatory phase is significantly prolonged beyond 14 days, pregnancy should always be suspected (See Figure 10). A persistent corpus luteum may also give rise to a prolonged

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NAME: E.B.

RECORD NO. Palmer

YEAR: 1947

MONTH: May

DAY: 1

DATE: 1

TIME: 1

TEMP: 1

WIND: 1

MOON: 1

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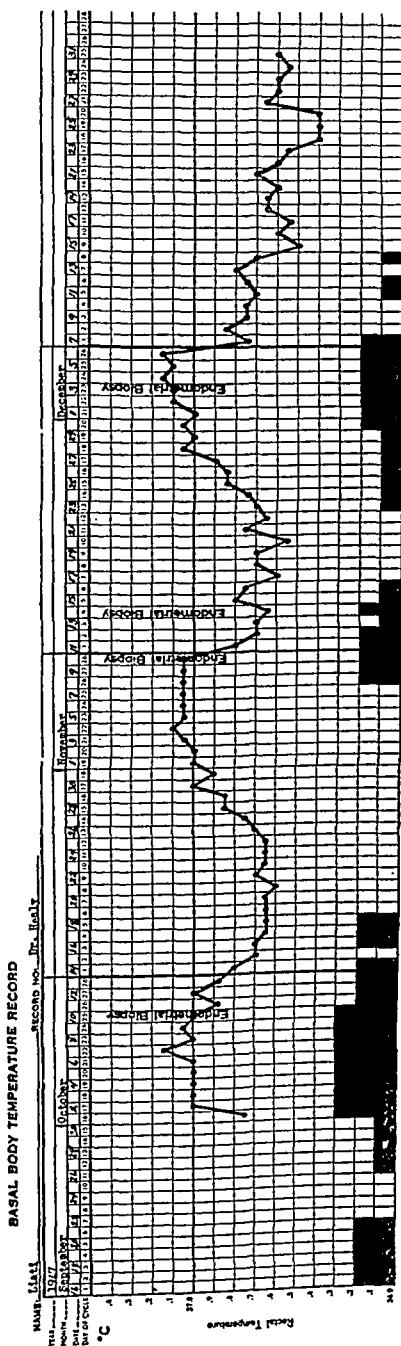


Fig. 9. Normal basal body temperature curve, but associated with menometrorrhagia. Endometrial biopsy specimens obtained 10 October, 10 November, and 3 December, 1947, reported as "incomplete shedding," were obtained during high temperature phases. On the basis of the onset of bleeding, the endometrial specimens were regarded as being obtained relatively early in the menstrual cycle but on the basis of the basal body temperature as shown they were obtained relatively late in the ovarian cycle. The endometrial biopsy specimen obtained 14 November during a low temperature phase contained no secretory gland elements. Estrogen by mouth was prescribed daily beginning the third day of a new cycle, 9 December, which suppressed bleeding and inhibited ovulation.

BASAL BODY TEMPERATURE RECORD

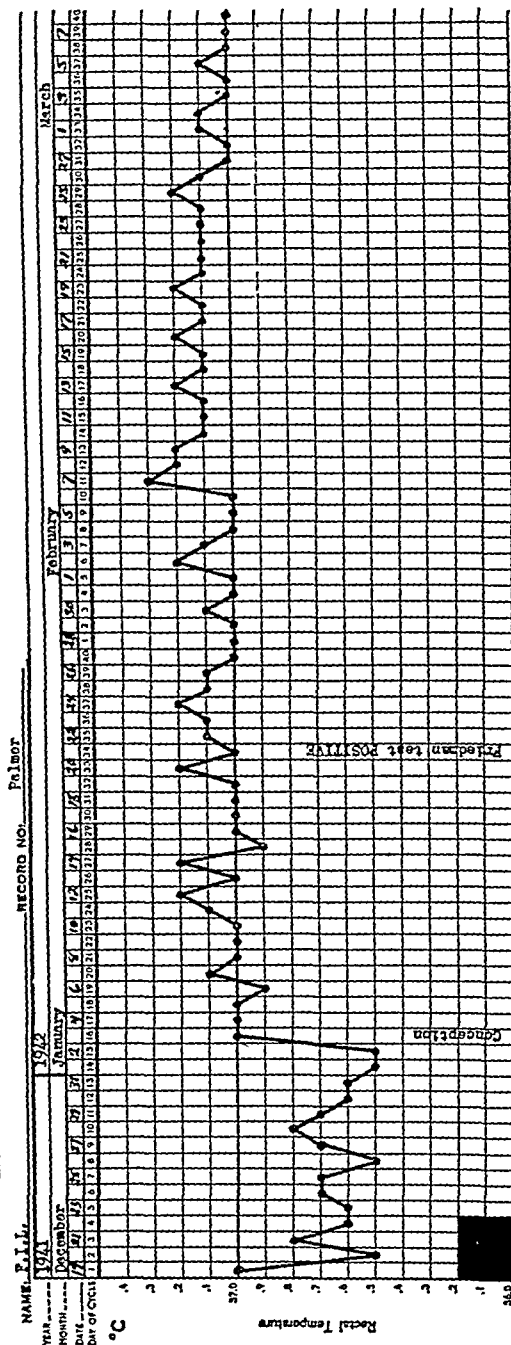


FIG. 10. Typical basal body temperature curve recorded by a patient during a menstrual cycle during which conception and the onset of normal pregnancy occurred about the 15th day of the cycle.

BASAL BODY TEMPERATURE RECORD

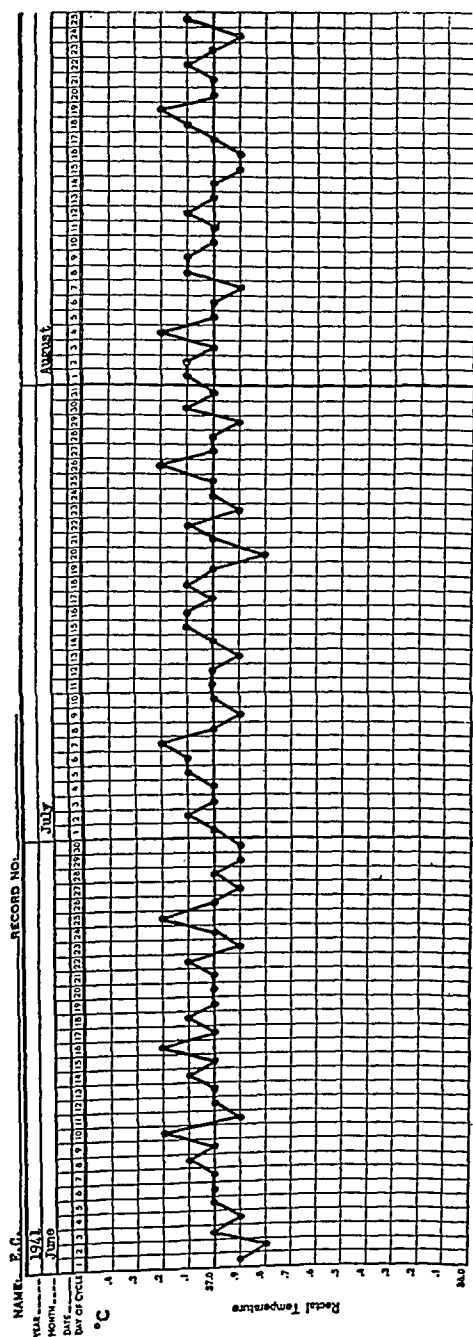


Fig. 11. Primary amenorrhea of anterior pituitary origin. Note persistently normal basal body temperature without cyclical fluctuations.

BASAL BODY TEMPERATURE RECORD

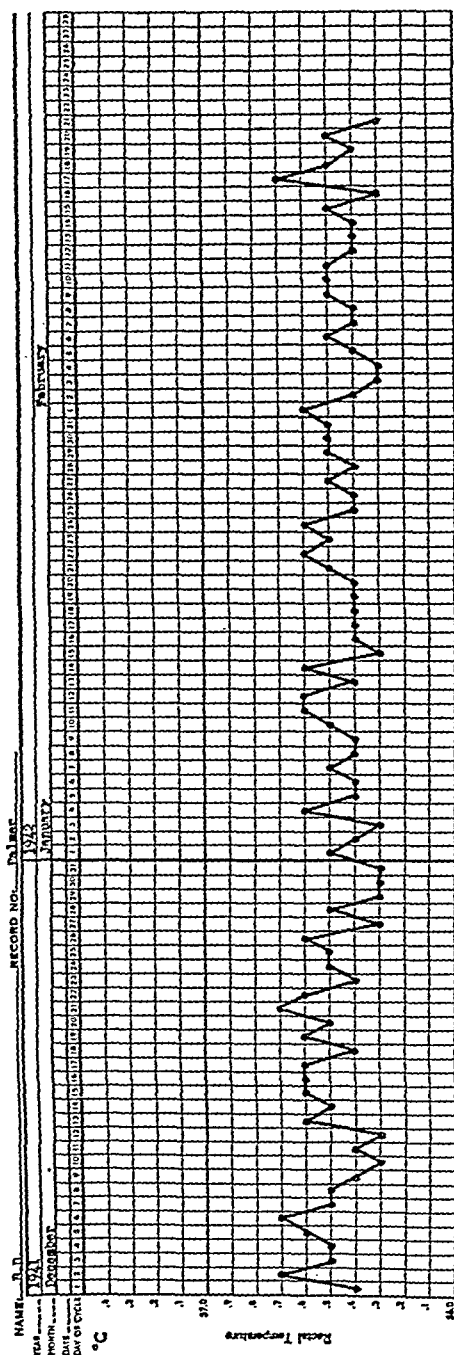


FIG. 12. Secondary amenorrhea due to persistent follicular activity. Note persistently low anovulatory type of basal body temperature.

BASAL BODY TEMPERATURE RECORD

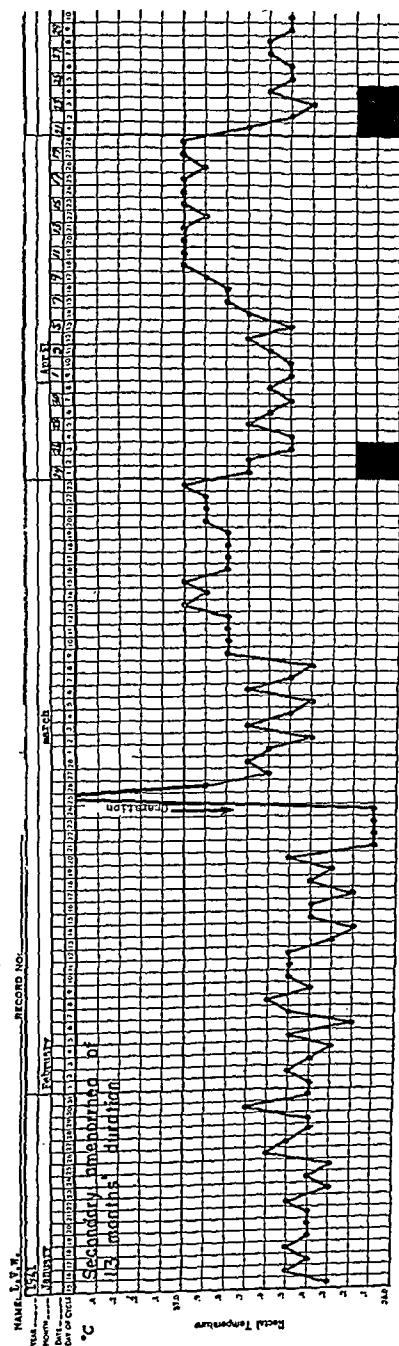


Fig. 13. Case of arrhenoblastoma: basal body temperature persistently low and anovulatory in type. Note that immediately following operation the basal body temperature became biphasic, indicating cyclical ovarian activity. The first menstruation in 16 months occurred 28 days after surgical removal of the ovarian tumor. (Palmer, 1942.)

post-ovulatory phase of the basal body temperature. No record of such a case is available at present, however. A prolonged post-ovulatory or high temperature phase associated with bleeding at the expected time of menstruation or at any time thereafter should lead to the diagnosis of a threatened abortion. After the diagnosis of pregnancy has been established, a sudden fall in the basal body temperature may precede the onset of a threatened or inevitable abortion.

Amenorrhea: The basal body temperature is acyclical at a *normal* level before puberty, in primary amenorrhea of pituitary origin (See Figure 11), in ovarian agenesis, and in secondary amenorrhea which occurs following bilateral oophorectomy or the natural menopause. It is acyclical at a *high* level during the amenorrhea of pregnancy (See Figure 10). It is acyclical at a *low* level in primary or secondary amenorrhea associated with persistent follicular activity (See Figure 12) "hyperestrinism" or "hyperhormonal amenorrhea" (Zondek, 1941), probably in patients with estrogen-producing granulosa cell tumors with or without amenorrhea, and has been observed in one patient with an androgen producing arrhenoblastoma (See Figure 13) (Palmer, 1942). The basal body temperature may *fluctuate normally* in amenorrhea due to stenosis or occlusion of the cervix, in amenorrhea associated with some cases of pelvic tuberculosis, or in patients with retained functional ovaries following hysterectomy.

Menorrhagia: The basal body temperature may fluctuate normally but show complete absence of synchronization between the menstrual fall and the onset of menstrual flow in severe cases of protracted premature bleeding described above and in patients with irregular bleeding associated with fibroids or polypi.

The basal body temperature may be acyclical and persistently low in patients with metropathia hemorrhagica or so-called "functional bleeding" due to hyperestrinism and hyperplasia of the endometrium. It is quite obvious that this condition is identical to that in patients with amenorrhea associated with similar endometrial pathology and that the same patients may have variable periods of amenorrhea and/or menorrhagia. The persistent proliferative type of endometrium observed is reflected in or indicated by the persistently low acyclical basal body temperature. When bleeding does occur there is not the normal complete shedding down to the basal glandular layer of the endometrium. The histological picture in either amenorrhea or menorrhagia may show marked hyperplasia and cystic changes in the endometrial glands.

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Obstetrics

PHYSIOLOGY OF PREGNANCY, LABOR AND PUERPERIUM

BLOOD GONADOTROPIN STUDIES DURING PREGNANCY IN RELATION TO THE FETAL SEX

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J. Clin. Endocrinol., 8: 600, 1948

In a series of 253 pregnant women, specific estrogenic and androgenic smears occurred in 37.5 per cent. Of these, 88.1 per cent were delivered of infants whose sex corresponded to the specific smear.

In a group of 64 women, blood gonadotropin assays carried out between the seventeenth and thirty-second week of pregnancy revealed a close relationship of the FSH:LH ratio and the sex of the infant.

The test is performed by the injection of 1 cc. of serum into immature female white mice both as whole serum and also in 3 dilutions over 3 days. At autopsy 48 hours after the last injection, FSH is estimated on the basis of ovarian stimulation, uterine weight increase and vaginal cytology, while the level of LH is established by the presence of hemorrhagic follicles or corpora lutea. A predominantly high level of FSH was associated with a female infant, while an equal level of LH and FSH was always followed by a male infant. When 3 cc. of the same serum was injected into immature female rats the same ratio of FSH to LH was obtained. Serum with a level of LH equal to FSH injected into immature male rats in the dose of 3 cc. produced descent of the testes and an increase in weight of the prostate, while serum with a predominantly high FSH titer failed to produce these results.

In those cases where a specific vaginal smear was obtained, the androgenic type was associated with a high LH titer, while the estrogenic smear occurred in the presence of an increased FSH level. Observations on a further group of 30 pregnant women are presented.

(The diagnosis of the sex of the fetus in utero shares with the diagnosis of pregnancy itself, the distinction of being the oldest problem in obstetrics. Thus we all will recall the often cited test of the ancient Egyptians as preserved in the Berlin Medical Papyrus: "To see if the woman is pregnant or not: barley and wheat are moistened daily with the woman's urine, like dates or pastry into bags. If they either generate, so she will give birth; if the wheat germinates, so it will be a boy; if the barley germinates, so will it be a girl; if they do not germinate, so she is not pregnant." Hippocrates was also interested in the question and said that "A woman with child, if it be a male, has a good color; if it be a female, she has a bad color." While freckles and blotchy skin indicated to the ancients a female fetus, pigmentation in general pointed to a boy; for instance, *lack* of pigmentation of linea alba below the umbilicus meant a girl.

These ancient writings not only attest the age-long curiosity which has been manifested in the sex of the unborn but advance concepts which, by a little stretch of the imagination, are in keeping with endocrine effects exerted by the fetal gonads. The whole history of the diagnosis of the sex of the human fetus in utero has been reviewed in an exhaustive and superlatively interesting fashion by Stuart B. Blakeley (*Am. J. Obst. & Gynec.* 34: 322, 1937). A perusal of Blakeley's scholarly study will prove rewarding as well as entertaining to any obstetrician.

The number of tests, supernatural and otherwise, which have been proposed for this purpose are myriad. They appear in all centuries and emanate from all peoples: Arabian, Indian, Chinese, Jewish, Russian, etc. The supernatural omens range from the prophetic interpretation of numerology, astrology and dreams, to the examination of entrails, the flight of birds and "ordeals." But Blakeley points out that the use of strictly supernatural means to diagnose fetal sex was never persistent or extensive, compared with what he calls "natural phenomena." These he divides into 3 broad groups:

Group 1. The supposed origin of the male from the right side of the uterus, the female from the left; and the changes in the right side of the pregnant woman's body ascribed to, or imagined to result from, such origin.

Group 2. The position, outlines, attitude and activities of the fetus during pregnancy and labor.

Group 3. The effects of a male fetus on the total maternal organisms; that is, the reactions of the female body to the introduction therein of a male element. This is the largest and most important group.

In regard to the first of these ideas, letters reach my office every once in a while purposing to acquaint me with the momentous secret of how a boy baby or girl baby may be prearranged; all that is necessary is to have the woman lie on the right side during coitus for a boy and on the left side for a girl,—the idea being of course that gravity will direct the spermatozoa to the proper ovary. Evidence of other sorts indicates that this old notion is more widespread among the gullible than is generally realized.

By far the best known of the second group of signs is the fetal heart rate. In 1859, on the basis of a study of 100 cases, Frankenhaeuser suggested that fetal sex might be determined by the rate of the fetal heart in the last 3 months of pregnancy, a persistently slow rate (averaging 124 or less a minute) indicating a boy, and persistently more rapid rate, (averaging 144 or more a minute) a girl. All obstetricians are acquainted with this old sign and practically all hold no brief for it,—if for no other reason because the fetal heart rate usually falls between the figures given.

As Blakeley has indicated, the last group of diagnostic methods is the most numerous and includes a wide variety of procedures from a modification of the Abderhalden test and vaginal Ph to the more modern endocrine approach. Quite a flurry in this field was raised in 1932 by Dorn and Sugarman who reported a method by which they claimed 94 per cent correct prognostications, 80 out of 85 cases (*J. A. M. A.*: 105: 1659, 1932). They injected intravenously into immature male rabbits, whose testes must be in the inguinal canals and not in the scrotum, the urine of women pregnant in the last trimester of pregnancy. If later examination of the testes of the animal showed increased vascularity and cellularity, and beginning spermatogenesis, they believed that they could conclude from their series of cases that the woman was pregnant with a female fetus. They thought that they had discovered, in the urine of a woman carrying a female child, a true and hitherto undiscovered sex "hormone which can stimulate the cells in the testicular tubules of the pubescent male rabbit and cause a precocious development." Very promptly, however, several papers appeared indicating that these claims could not be confirmed (*Daily: Am. J. Obst. & Gynec.* 27: 721, 1934; Pommerenke and Rogers: *Idem* 30: 380, 1935; Murphy and DeRenye, *Endocrinology* 18: 521, 1934). And in the main, the same fate has befallen all tests thus far proposed.

The failures which have been reported thus far in this field have not been reviewed to engender skepticism about this most recent report of Nieburgs and Greenblatt, or in any way to discourage them, but rather to call attention to the widespread and abiding interest

which this subject has evoked. In other words, it would be quite an accomplishment if these authors could answer this ancient riddle and I hope they can.—Ed.)

THE RENAL CLEARANCE OF CHORIONIC GONADOTROPIC HORMONE IN PREGNANCY AND IN NEOPLASM OF THE TESTIS

C. F. GASTINEAU, A. ALBERT AND L. M. RANDALL

Mayo Clinic, Rochester, Minnesota

J. Clin. Endocrinol., 8: 599-600, 1948

The concentrations of chorionic gonadotrophin in the serum and the urine of human subjects were determined, and the renal clearances were calculated. A total of 20 such clearances were made on 5 normal pregnant women and one on a patient with chorionepithelioma of the testicle. The average clearance in pregnancy was found to be 0.38 ± 0.14 ml./min.; that for the first trimester, 0.44 ± 0.10 ml./min.; that for the second trimester, 0.37 ± 0.17 ml./min.; and that for the third trimester, 0.36 ± 0.10 ml./min. Thus, clearance was relatively constant during all stages of pregnancy although the serum and urinary concentrations exhibited as much as a twenty-fold variation.

The concentrations of hormone in the patient with testicular tumor were: urine, 9.6 I.U./ml.; serum, 28 I.U./ml.; and neoplastic tissue, 220 I.U./Gm. The clearance was 0.23 ml./min., a value in the lower limit of those found in pregnancy.

These studies show that the normal human kidney clears chorionic gonadotrophin in a relatively constant rate. Furthermore, results indicate that with normal renal function, changes in urinary excretion are reflections of changes in serum level and therefore probably depend mainly on changes in rate of production of the hormone.

(This is a valuable contribution to a fundamental problem and it is hoped that the authors will augment these studies by observations on patients with preeclampsia. The reports of the Smiths would seem to indicate that there is some lag in the secretion of chorionic gonadotrophin in patients who develop toxemia. Thus they say that "The urinary values for the anterior pituitary-like hormone do not rise to abnormal levels until toxemia has become clinically manifest, whereas excessive amounts in the serum are demonstrable 4 to 6 weeks prior to the development of toxic signs." (Am. J. Obst. & Gynec. 38: 618, 1939.) The Smiths believe that the most plausible explanation of this phenomenon lies in a failing utilization of anterior pituitary-like hormone in the production of progesterone and estrogen and consequent building-up of the level of anterior pituitary-like hormone in the blood. Gastineau, Albert and Randall now state that the normal kidney clears chorionic gonadotrophin with relative constancy during all stages of pregnancy, although the serum and urinary concentrations may show as much as a 20-fold variation. The building-up of chorionic gonadotrophin in the serum which the Smiths speak about is obviously at variance with this observation of constant clearance unless it can be demonstrated that the kidney in oncoming preeclampsia develops a serious inability to excrete this hormone. This whole problem of the hormones in the toxemias of pregnancy impresses me as being in a confused and unconvincing state and it is hoped that further studies such as the above will help elucidate it.—Ed.)

MANAGEMENT OF NORMAL PREGNANCY, LABOR AND PUERPERIUM

SHOCK DURING CONTINUOUS CAUDAL ANESTHESIA: CASE REPORT

A. J. KELLEY

Savannah, Georgia

Current Researches in Anesth. & Analg., 27: 236-239, 1948

In 604 cases in which caudal anesthesia has been used by the author, shock has occurred in varying degrees on 3 occasions. Two of these cases are reported in this paper in some detail.

The first patient, aged 35 years, secundipara, was to have an elective cesarean section because of a previous stillbirth due to prolonged labor resulting from bony disproportion. She received 70 cc. of 1.5 per cent metycaine in the caudal space over a period of 12 minutes. Thirteen minutes later the level of skin anesthesia had reached the fourth thoracic segment and the patient showed definite evidence of shock. Following subcutaneous use of ephedrine and intravenous use of 5 per cent glucose and ephedrine, signs of shock subsided and the operation was completed without further complication.

The second patient was an 18-year-old primipara in whom cesarean section was to be done because of a justo minor pelvis. She received 60 cc. of 1.5 metycaine over a period of 23 minutes and 10 minutes later the operation was begun. On opening the peritoneal cavity, signs of shock ensued and despite intravenous use of plasma and ephedrine the patient's condition remained poor and the operation was postponed. After recovery from shock she was returned to the operating room and a cesarean section was performed under cyclopropane anesthesia.

In retrospect, the author feels that several errors were committed which contributed to the shock. The first of these was that a prophylactic dose of ephedrine was not given prior to operation in these cases. Secondly, insufficient time elapsed between the second and third dose of metycaine to establish the level of anesthesia. Thirdly, it is felt that the metycaine was injected too rapidly and under too great pressure. Estimation of the proper pressure for injection of the drug comes only with experience in using this type of anesthesia. Lastly, the abdomen should not be opened until a sufficient period of time has elapsed to allow for stabilization of the patient.

(Case reports which emphasize caution in the development of new technics in medicine, and particularly anesthesia, are more important in the safe development of such technics than most enthusiastic reports. Doctor Kelley has emphasized one of the 2 most consequential complications with caudal analgesia, namely: critical hypotensive states resembling shock.

The severity of this shock-like state in all forms of regional conduction anesthesia is in direct proportion to the number of white rami communicantes of the sympathetic vasomotor system which are blocked. Thus, the flood gates of the circulatory system are segmentally opened. Hypotension, diminished cardiac venous return, hypoxia, anoxia, and irreversible shock become the ultimate end point unless this pernicious deterioration is offset. Hypotension itself, which accompanies more than half of the nerve blocks with spinal and caudal anesthesia adequate for cesarean section, can be prevented or promptly treated if the safeguards described in the previous editorial note are rigidly adhered to.

In both cases under consideration the doses of the caudal anesthetic were large and were injected over too short a period of time. The hypotensive state could have been prevented in both instances by the preanesthetic administration of 500 cc. of 5 per cent glucose containing 25 mg. of ephedrine to continue in a slow intravenous drip during the operation. All of the pioneers who have developed extradural anesthesia, both through the caudal and the lumbar peridural approach, have emphasized that a safe waiting time of from 20 to 40 minutes following administration of the anesthetic is necessary to provide intense conduction block. Should the obstetrical emergency demand a more prompt entry into the uterus, a more rapid anesthetic such as continuous spinal or pentothal and oxygen is to be preferred. The extradural block, however, is an excellent one for the poor risk patient and for the one fatigued after long hours of nonproductive labor. In such cases it is sometimes good practice to institute the block slowly one to four hours before section to provide physiologic rest and regulation of body fluids.

These two cases reported here, and others recorded in the rapidly increasing literature on the subject, sound the warning that this form of anesthesia is efficient and safe only in the hands of the obstetrician-anesthesiologist who understands the pharmacology of the drug, the altered physiology of the patient, and the regional anatomy upon which the technic of caudal analgesia has been established.—Robert A. Hingson)

FATALITIES FROM SPINAL ANESTHESIA

J. ADRIANI

New Orleans, La.

South. Surgeon, 14: 506-518, 1948

In a period of 7 years, 14 deaths were encountered in a series of 12,500 spinal anesthetic blocks. In all of these cases death was obviously caused by the spinal anesthesia alone or the anesthesia appeared to play a distinct role. Death in 12 cases resulted from circulatory collapse and in 2 cases from respiratory paralysis. Respiratory paralysis results from gravitation of the anesthetic agent high up in the spinal canal. This can be prevented by sharply flexing the head on the shoulders, repeated testing of the level of anesthesia and by preventing shifting and straining of the patient which may cause compression of the dural sac and force the drug higher in the spinal canal.

The mechanism of circulatory collapse is not always clear but apparently it is the result of a combination of factors, all of which lead to pooling of the blood in the viscera. Primary cardiovascular disease may predispose the patient to circulatory collapse. In generalized arteriosclerosis, circulatory adjustments do not occur readily, and circulatory depression may be difficult to overcome.

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The recent reported experiences of Clifford Lull and J. C. Ullery, reporting 1000 consecutive continuous spinal anesthetics for cesarean section without maternal mortality, indicates that death from spinal anesthesia in even seriously handicapped patients is unnecessary (*American Journal of Obstetrics and Gynecology*, in Press). We substantiate this experience with an additional 600 consecutive continuous spinal anesthetics for cesarean section without maternal mortality.

As Adriani ably points out, the choice of spinal anesthesia in shock and in hypotensive states is a disastrously incorrect one. It should be emphasized, however, that when contraindications for other types of anesthesia exist in this group of cases, it is possible to correct the hypotension before the anesthesia starts with intravenous fluids and vasopressor drugs. When these prophylactic measures are augmented by the inhalation of enriched oxygen atmospheres, the severely crippled cardiac patient, the hypertensive and toxemic patient, the patient with respiratory, renal, and metabolic disease, tolerate spinal anesthesia well according to the dosage schedule listed above.

Since it has been established that spinal anesthesia and related forms of conduction anesthesia can be utilized in thousands of cases without mortality, it becomes significantly the duty of the medical centers which train young physicians, and pharmaceutical firms which supply anesthetics and dosage schedules, to teach proper dosage and proper technic. —Robert A. Hingson.)

CONTINUOUS CAUDAL ANALGESIA

W. H. MASTERS

St. Louis, Mo.

Am. J. Obst. & Gynec., 56: 756-761, 1948

In order to evaluate continuous caudal analgesia when given by resident physicians, a report is made of 1,500 patients whose labors were conducted under continuous caudal analgesia administered exclusively by the house staff. A comparison would then be possible with the published reports of more experienced persons.

The success of each caudal was given a grade ranging from 100%, when pain was completely relieved between the time when the level of analgesia was reached and the delivery and repair were completed, to 0%, when no analgesia was established at all. Grades of 90% or better were successful, 50% to 80% were partially successful, and those below 50% were termed failures. Successful cases were 83.5% of the total, partially successful were 3.8%, and failures were 12.7%.

There were 191 failures in the group. In 98 cases the needle could not be correctly inserted. This was 6.5% of the total attempts. In 17 cases the needle either slipped out or the tube became disconnected. Ten failures were due to faulty anesthetic agent and another 10 failures showed the caudal satisfactory but the patient too emotionally unstable to permit continuation.

The effect on the child was studied. The promptness of the spontaneous cry and respiration was noted. Only 2.5% of the mature infants required any resuscitative measures. Resuscitation in the premature group was 6.0%.

Patients with anemia do not tolerate spinal anesthesia well, probably because tissue anoxia is more prone to occur if circulation is depressed. Increased intra-abdominal pressure, whether caused by distention from intestinal obstruction, ascites or large ovarian tumors, often predisposes to severe circulatory collapse. Perhaps this is due to compression of abdominal veins with resulting retardation of return of blood to the heart. The obstetrical case will also often show marked hypotension following spinal anesthesia. Strangely enough, the blood pressure suddenly improves as the infant is delivered.

Patients in shock obviously do not withstand spinal anesthesia, regardless of the origin of the shock. Patients who have recently recovered from shock are also poor candidates for this type of anesthesia. The collapse precipitated by spinal anesthesia is neurogenic in origin, and responds to vasoconstrictor drugs.

Nupercaine, pontocaine and procaine were all used in this study. There is no difference in potential hazards of these drugs except that when difficulties arise while using the longer acting nupercaine and pontocaine, their effect persists over a longer period of time. Toxic reactions occur only if an excessive amount of the drug enters the blood stream. The difficulties encountered in spinal anesthesia are due to extensiveness of anesthesia and completeness of motor paralysis and not to toxicity.

(This significant report from the Department of Anesthesia of the Charity Hospital should be studied by all physicians who administer spinal anesthesia. Adriani has carefully emphasized the safeguards necessary in the minute-by-minute protection in this group of patients. Likewise, he has emphasized the tragic results from the omission of the safeguards or from the commission of anesthetic error. Of primary significance is the fact that spinal anesthesia dosage made standard by widespread usage is entirely too high for the average case. In this series of 14 deaths 7 occurred within the first 20 minutes. Five of these 7 received from 15 to 20 mgms. of pontocaine as a single injection anesthetic. Two of these 7 deaths were caused by ascending respiratory paralysis.

Experience with continuous fractional dose spinal anesthesia has taught us that all of these patients could have been spared respiratory and circulatory collapse had they been given smaller doses of the anesthetic agent. A few of them could possibly have been rescued had lumbar puncture and drainage of 10 to 15 cc. of cerebral spinal fluid been instituted in the midst of these dire emergencies. *In both of the cesarean sections the doses of pontocaine as a spinal anesthetic were entirely too high* and were based on the surgical rather than the obstetrical standard. From accumulated experiences in the literature and from the analysis of these two spinal anesthetic deaths preceding contemplated cesarean section, we are able to postulate emphatically a maximum dosage in a single administration for this operation: pontocaine, never more than 8 mgms. for cesarean section, nor more than 5 mgm. for vaginal delivery; procaine, never more than 75 mgm. for cesarean section nor more than 40 mgm. for vaginal delivery; nupercaine, never more than 6 mgm. for cesarean section nor more than 4 mgms. for vaginal delivery; metycaine, never more than 50 mgm. for cesarean section nor more than 30 mgm. for vaginal delivery.

If it is anticipated that the operation will outlast the pharmacologic effects in the control of pain of this dosage schedule, then it is the duty of the anesthesiologist to utilize the safer continuous technics.

The overwhelming hazards of the dosage scale used in all of these fatalities can be readily appreciated from the fact that individual doses of 5 mgm. of pontocaine, 30 mgm. of procaine, 2½ mgm. of nupercaine or 22 mgm. of metycaine, administered as single dose spinal anesthetics between lumbar III and IV have each given inclusive areas of somatic anesthesia from the fourth thoracic segment downward in both obstetrical and surgical patients.

England Journal of Medicine, 239: 429-433, Sept. 16, 1948.) The normal baby in utero at this same time manifests its lowest ebb in reflex activity. The medullary nerve centers of the premature baby are the most sensitive human tissues to pharmacologic intoxication and depression.

Obstetricians cognizant of these phenomena and of the traumata concomitant with premature labor and delivery are generally supporting the thesis of Masters in choosing continuous caudal analgesia for the premature.

It is significant also that Masters and his group found this technic of advantage in controlling the extremes of hypertension, both in severe pre-eclampsia and in eclampsia with convulsions.

This paper furthermore emphasizes the important role of the house staff in understanding, initiating, and maintaining this highly specialized form of conduction anesthesia. As these technics develop, it becomes more necessary for the resident in obstetrics to familiarize himself with the pharmacologic dosage and anesthesiologic technics that are applied regularly in the safe conduct of labor and delivery.—Robert A. Hingson.)

Results in the premature group were striking. There was a mortality rate of 3.96%. For comparison, records of labors conducted without caudal analgesia and resulting in premature infants during the same period of time as the caudal group were analyzed. Of the 101 babies living at the onset of labor in the caudal group the mortality percentage was 3.96%, and of the 225 babies in the non-caudal group the percentage was 14.66%. Although there was a slight tendency to use caudal analgesia in a premature birth, the frequency of premature births in both groups was about equal. Results indicated that the use of the caudal increased the probability of the premature infant living through labor and reaching the nursery. Their ultimate chances of survival were considerably greater also. In the caudal group only 3.96% died neonatally and in the non-caudal group 8.88% died. The significance of these results was explored. All infants were born in the same time period and cared for in the same nursery. When the two groups were divided into chronological halves the incidence of mortality within each group remained consistent. Thus the author feels that these results can be considered significant.

The safety of the method is discussed. The needle broke in 3 cases, necessitating a short skin incision. In 2 cases an occult subarachnoid tap resulted in a spinal anesthesia. Infection at the site of the puncture occurred in 5 cases. In 17 cases the blood pressure was so labile that the caudal was discontinued.

One of the most undesirable features of caudal analgesia is the fall in the blood pressure. In 30% of the cases systolic pressure fell to 90 mm. Hg. and in 13.6% cases it fell to 80 or below. In the majority of cases the blood pressure returned to normal when the patient's position was changed. It was learned that there were fewer cases of severe depression if the induction was carried out with the patient on her back and that then she could easily be moved to her side, if necessary.

There were only 2 cases of maternal mortality and neither was in any way due to the type of analgesia used. The 1,500 cases included several difficult problems such as pre-eclampsia, eclampsia, tuberculosis, asthma, and acute respiratory disease. Caudal analgesia was given to almost all cases with heart disease, including one with coarctation of the aorta and 3 with advanced rheumatic heart disease. Each of these was delivered without incident.

The author concludes that the risk to the mother in continuous caudal analgesia is no greater than the risk of other forms of analgesia. The risk to the baby is no greater and to the premature infant it appears to be materially less.

(The obstetrical department of the Barnes Hospital has conclusively presented both the advantages and disadvantages of continuous caudal analgesia in its own significant experience.

The protection afforded the premature baby during labor and delivery with this technic is sufficiently documented in this report to recommend this method among the best for such cases. Certainly it points out that the control of maternal pain for the delivery of the premature baby is no longer necessary through the use of dangerous depressive narcotic agents and systemic anesthetics. Hershenson of the Boston Lying-in Hospital has pointed out that the mother in the midst of uncontrolled labor pain is at the acme of nervous reflex excitability. (Hershenson, Bert B.: Premedication and Anesthesia in Obstetrics, New

which the author has now substituted pentobarbital of sodium or sodium phenobarbital for chloral, and have continued morphine, intravenous glucose and molar lactate. Eleven of the 25 fetal deaths occurred in these 61 patients. Sixty-three patients were started on a modified Stroganoff regime on admission and 13 of the fetal deaths occurred in that group. In the 3rd group, 13 patients had their first elevation of blood pressure when admitted in active labor and had no treatment. Twelve of these delivered vaginally with 1 fetal death in a patient who was in labor for 98 hours and had intrapartum infection and a contraction ring.

Labor seems to have a more marked effect on the blood pressure of a toxemia patient than on that of a normal patient. Time after time the author has seen sharp, sudden rises of blood pressure to dangerous levels during labor in patients who were improving under treatment, or whose slight elevation of blood pressure was not considered enough to warrant admission and treatment. Thirty-one of the 137 patients were delivered by cesarean section and 106 were delivered vaginally; all the sections except 1 were done for severe preeclampsia. In the previous series, 27 cesarean sections were done in 290 cases; 6 of these operations were done for reasons other than severe preeclampsia. The author and his associates, therefore, are performing 3 times as many sections for this condition as they did in the first 10 year period.

The author wishes to call particular attention to 2 weight groups, 1000 to 1499 grams and 1500 to 1999 grams. There were 11 deliveries by cesarean section in these groups with 3 fetal deaths, and 13 vaginal deliveries with 10 fetal deaths, making a total of 13 deaths in 24 cases.

The author believes that the only treatment for the fulminating cases is immediate delivery, and judging by his results in other severe cases of preeclampsia he recommends a more radical approach to these cases after severe preeclampsia is diagnosed. A baby in the 1000 to 1999 gram weight group has a much better chance if delivered promptly. If the patient is over 32 weeks pregnant, the rate of survival of her baby is higher when there is no delay in delivery.

In the opinion of the author, the modern treatment of severe preeclampsia and eclampsia is excellent insofar as the mother is concerned. Combining his 2 series he reports a total of 58 cases of eclampsia with 1 maternal death. In the same 17 year period, 424 cases of severe preeclampsia were managed with no maternal deaths.

A gross fetal mortality for the 2 conditions, that is preeclampsia and eclampsia, of 20.7 per cent in the first period and 17.3 per cent in the second, should certainly be drastically reduced, according to the author's belief. Prompt delivery of patients once the diagnosis is established appears to be one way to bring about a lowered fetal mortality. If the patient is 32 weeks or more pregnant, the baby seems to do well regardless of its weight if not allowed to stay in utero too long. Severe preeclampsia, even in the face of improvement, causes fetal death. With modern facilities for the care of the premature baby, it is no longer necessary to wait and wait for the baby to attain a certain estimated weight. Elimination of the term 'mild preeclampsia' in hospitalized patients

PATHOLOGY OF PREGNANCY

RESULTS IN THE TREATMENT OF SEVERE PREECLAMPSIA

CHARLES M. McLANE

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M. Rec. & Ann. 42: 669-672, Nov. 1948

In 1943 Dr. Katherine Kuder and the author reported all the cases of severe preeclampsia and eclampsia which had occurred in the Woman's Clinic of the New York Hospital from September 1, 1932 to December 31, 1942. There were reviewed in that paper 290 cases of severe preeclampsia, and certain definite suggestions and recommendations were made: 1. Patients who do not respond to conservative therapy might be delivered earlier, thus decreasing the fetal mortality rate; 2. The fulminating type of severe preeclampsia as a rule improves only with delivery.

The present study, a review of all cases of severe preeclampsia and eclampsia occurring from January 1, 1943 to June 30, 1947 in the same clinic, was undertaken to see whether their results were improved by following these suggestions. In addition to cases of severe preeclampsia the author includes those cases of eclampsia which represented failure in his treatment of severe preeclampsia, the entire series reported comprising 9 cases of ante- or intrapartum eclampsia and 137 cases of severe preeclampsia. The incidence of severe preeclampsia agreed closely with that reported in their earlier series, namely, 0.87 per cent.

The author first discusses the 9 cases of eclampsia in the series. There were no maternal deaths and only 1 fetal death in this group. The 1 fetal death occurred in a patient 37 weeks pregnant who had had 2 convulsions before admission, the fetal heart never heard in the hospital, and who delivered a macerated fetus 31 hours after admission. Four of the 9 eclamptic patients were delivered by cesarean section after each had gone 36 hours without a convulsion and with improvement; all these babies survived, including 1 which weighed only 960 grams.

There were 137 cases of severe preeclampsia with no maternal deaths. Twenty-five fetal deaths in 141 babies delivered (4 sets of twins) showing a mortality incidence of 17.7 per cent as compared with 19.5 per cent in the previous paper. The gross fetal mortality, including the 9 eclamptic patients, was 17.3 per cent as compared with 20.7 per cent in the earlier series reported.

The type of treatment fell into 3 categories. Sixty-one patients were considered either to have mild preeclampsia, or, even though showing symptoms of severe preeclampsia, were treated as mild, that is, by bed rest, light sedation and a low protein, low salt diet. Some of these who became progressively worse were later treated by the second method, that is the modified Stroganoff in

sedation, salt poor diet, intravenous glucose, etc., will often convert a poor operative risk into a moderately good one. For this reason it is my feeling that no case of preeclampsia, no matter how severe, should be subjected to operative procedure, either section or induction, before 24 hours of rest and medicinal therapy has been instituted. We have killed at least 1 extremely severe preeclamptic by failure to observe this rule and I am sure that McLane would be the first to agree that rushing into these sick women, "right off the streets," as it were, is a good way to kill others.

But these reservations in no way controvert McLane's general thesis. His contention that in severe preeclampsia the outlook for the baby at all gestational ages is better outside the uterus than within, is generally valid, it seems to me; but it should be noted that a large proportion of his fetal losses occurred in cases which were regarded as "mild." This reminds us that mild preeclampsia is a stage in a grave disease process and that, despite

TABLE 7

Incidence of induction of labor for preeclampsia by 5-year periods, January 1, 1924 to December 31, 1943

PERIOD	CASES OF PREECLAMPSIA	INDUCTIONS	%
1924-1928	238	41	17.2
1929-1933	563	82	14.6
1934-1938	545	69	12.7
1939-1943	1,072	167	15.6

TABLE 8-B

Analysis of 167 inductions (171 infants)

FETAL MORTALITY	INFANTS	STILLBORN	NEONATAL DEATHS	TOTAL INFANT MORTALITY %
Mature (2500 Gm. +).....	138	0	1	0.7
2000 to 2499 Gm.....	25	3	0	12.0
1500 to 1999 Gm.....	5	1	1	40.0
1000 to 1499 Gm.....	3	1	1	66.6
Total.....	171	5	3	4.7

the adjective, a woman suffering from it may at any time have fetal death in utero, or indeed convulsions. Then, there is another way of looking at these cases. If pregnancy is terminated early in severe preeclampsia, even though the baby be lost, the patient's outlook for successful childbearing in the future is much better than if the hypertensive process had been allowed to drag on until the patient is left a chronic hypertensive. This statement can be documented in any large series of preeclamptics whose later pregnancies are studied.

But if it be granted that termination of pregnancy in preeclampsia is often desirable, the question arises: How is this best to be done? McLane emphasizes the increasing employment of cesarean section for preeclampsia at the New York Hospital to the exclusion of any mention of induction of labor. As may be seen in Table 7 (from the article mentioned above) the incidence of induction for preeclampsia in our own hospital has been surprisingly constant over the past 20 years, namely, around 15 per cent. We feel that it has an important place in the management of many of these cases, both mild and severe, especially those near term, provided a little judgment and common sense are employed. McLane's fear that the blood pressure will go up in labor is well justified and in very fulminating cases

and the freer and more prompt employment of cesarean section under local anesthesia might easily cut the fetal mortality in half.

(This paper deals with one of the most frequent and perplexing problems with which the obstetrician has to deal, namely, the management of preeclampsia from the viewpoint of fetal salvage. From the standpoint of the mother's immediate and ultimate prognosis, there is agreement that, in general, the sooner the pregnancy is terminated the better. However, because the baby may be premature, the tendency is widespread to temporize in many of these cases in the hope that a few more weeks of intrauterine life will give the infant a better chance. In this paper McLane advances the opinion that even for the sake of the baby, such a waiting policy is ill-advised since preeclampsia itself may kill the child and hence, even in the lower weight brackets, the likelihood of its survival in severe preeclampsia is better outside than inside the uterus.

TABLE 6

Days of hospitalization prior to delivery in cases of preeclampsia, 1939-1943

	CASES	%
Cases of preeclampsia in period.....	1,072	100.0
Admitted because of preeclampsia before onset of labor.....	510	47.6
Admitted in labor.....	562	52.4

Days of hospitalization in 510 preeclamptic cases admitted before onset of labor

DAYS	CASES	%
1- 5	431	84.5
6-10	46	9.0
11-15	16	3.1
16-20	9	1.8
21-25	5	1.0
26-30	3	0.6

In an investigation of preeclampsia (both mild and severe) carried out by Steptoe and myself a few years ago, it was demonstrable that our policy at the Johns Hopkins Hospital has been in keeping with McLane's recommendation, as may be seen from Table 6 of that study (Eastman and Steptoe: *Canad. M. A. J.* 52: 562, 1945). Among 510 preeclamptic patients who were not in labor but who were admitted because of this complication, 431 or 84.5 per cent were delivered within 5 days of entry and 93.5 per cent within 10 days. As a matter of fact, we were rather surprised to see these statistics because no outright or overall attempt had been made to hurry these patients except as may have been dictated by ordinary clinical judgment in individual cases. The manner in which early birth was effected in the 431 patients who delivered within 5 days was: spontaneous onset of labor, 185; artificial rupture of the membranes, 142; cesarean section, 66; medical induction (in the old days) 37; hysterotomy before viability, 4; hysterectomy, 1; and vaginal abortion, 1. The fact that so many of our patients went into labor spontaneously within a few days after admission brings to mind one advantage of a waiting policy, at least in mild cases near term, namely, the ever present possibility that spontaneous onset of labor may settle the problem very happily for all concerned. Another advantage of temporizing for a short while in these cases, and a paramount one, is the fact that a day or two of complete rest,

through the use of caudal analgesia, veratrum viride or by allowing sufficient time to elapse for a normal drop in the blood pressure. As the blood pressure was lowered by any of these methods, the convulsions ceased and the clinical picture markedly improved.

In every case changes in the EEG were associated with drop in blood pressure, regardless of what caused the drop. Slow, high voltage activity was replaced by the more normal low voltage, faster material as the blood pressure fell. When the blood pressure did not change the EEG did not show any improvement. Convulsions were controlled and clinical improvement was observed with the drop in blood pressure and the improved EEG pattern.

There has been experimental evidence which demonstrates the changing pattern of the EEG associated with changes in the arteriolar size in the cortex. Artificially produced hypertension has also led to convulsions of the grand mal type. From this experimental evidence plus the reported clinical observations, the author suggests that perhaps angiospasm plays an important role in eclamptic convulsions. 3 figures.

(When electroencephalographic studies were first made in eclamptic patients it was hoped that this procedure might prove of value in forecasting the onset of eclampsia in preeclamptic patients by the demonstration of brain waves characteristic of the convulsive state. Unfortunately, this hope has not been fulfilled. Thus, in the original article by Jost which gives in detail the history of his only case reported in which an EEG was obtained prior to convulsions, it is clear that the electroencephalographic record was entirely normal 3 days before the eclamptic attack, despite the fact that the patient was then suffering from preeclampsia. Hence, it does not appear to be possible by this means to spot those preeclamptic gravidae who are especially likely to develop convulsions.

There can be no question that the brain waves of patients in the actual eclamptic state, that is when they are experiencing convulsions and coma, are decidedly abnormal. These are very clearly shown in the original article as being, for the most part, slow waves, about 2 per second, and of large amplitude. It is well known that these slow dysrhythmias are seen in various pathological conditions associated with coma.

It is the contentio of the author that these abnormal brain waves in eclampsia, that is, the "high voltage, slow activity" patterns parallel the blood pressure. Since the recovery of any eclamptic patient from convulsions and coma to normal cerebration is usually paralleled with a return of the blood pressure to figures which approach the normal, it would be expected that the brain wave improvement would also parallel the blood pressure decline, since the electroencephalogram is merely a record of functional activity of the cerebrum. This is tantamount to saying that lines parallel to the same line (clinical improvement) are parallel to each other.

Whether the brain waves improve *because* the blood pressure declines, as the author believes, is a different matter. Although an approximate and possibly indirect relationship must exist here, and certainly all would agree with his angiospasm theory, it is to be questioned if the relationship is as direct and clearcut as Jost indicates. For instance, in his case 2, the final record was run 12 days after the eclamptic attack and showed a return to "a relatively normal pattern." Yet the blood pressure at that time was still 154/114,—this in a 19 year old girl. Contrariwise, in another case (No. 9), although the blood pressure was reduced from 220/145 to 82/60 by caudal anesthesia, only a slight improvement was observed in this EEG.

It is the opinion of many competent observers that the cerebral disturbances seen in eclampsia are due immediately to cerebral edema and it would be my guess that the EEG follows this rather than blood pressure alterations.—Ed.)

may even swing the decision to abdominal delivery despite a favorable cervix. However, the great majority of these cases near term, even though severe, can be managed safely with induction provided the patient is protected against convulsions during labor either with magnesium sulfate or conduction anesthesia. Our fetal mortality, as shown in Table 8-B, in 167 inductions done for preeclampsia, has been very low in term babies, but in premature infants the results have not been quite as good as with cesarean section. This is brought out if the former table is compared with Table 10-E which shows our fetal mortality

TABLE 10-E
Analysis of 71 Cesarean sections (75 infants)

FETAL MORTALITY	INFANTS	STILLBORN	NEONATAL DEATHS	TOTAL INFANT MORTALITY %	CORRECTED FOR PREMATURE SEPARATION
Mature (2500 Gm. +)...	26	1*	0	3.8	0.0
2000-2499 Gm.....	25	0	2	8.0	8.0
1500-1999 Gm.....	13	2*	3	38.5	23.1
1000-1499 Gm.....	11	0	4	36.4	36.4
Total.....	75	3	9	16.0	12.0

* Fetal death before operation due to premature separation of the placenta. In 5 other cases cesarean section was performed because of this indication in addition to preeclampsia. One was a twin pregnancy. Of the 6 infants involved, 1 died in the neonatal period while 5 were discharged in good condition.

in 71 cesarean sections performed because of preeclampsia. Although both these tables carry a large sampling error, they are in keeping with McLane's contention that cesarean section gives somewhat better results for the premature infant in cases of preeclampsia.

Finally, I cannot help but express surprise over McLane's statement that a low protein diet has been used in his cases of preeclampsia over the past 5 years. This is so contrary to current trends that I am even wondering if it is not due to a misprint in this otherwise excellent article.—Ed.)

ELECTROENCEPHALOGRAPHIC RECORDS IN RELATION TO BLOOD PRESSURE CHANGES IN ECLAMPSIA

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Am. J. M. Sc., 216: 57-63, 1948

Thirty-three electroencephalographic records were obtained before, during and after eclamptic convulsions in 9 cases. Special attention was paid to the changes in the EEG and the improvement in the clinical picture when the high blood pressure, which was associated with the toxemia, was lowered either

doses had no effect on sodium excretion, but with the larger doses a definite increase in urinary sodium was found. This was true despite the fact that the aminophyllin occasionally produced vomiting, with additional sodium loss in the vomitus.

Mercurials and mercurial-theophyllin compounds were also investigated. Small doses of mercurials (2 cc.) were often ineffectual, but larger doses (3-4 cc.) produced marked increase in both the urinary volume and the total sodium excretion. The effect of the mercurial-theophylline compounds closely paralleled the action of mercurials alone. In both drugs there was often a slight retention of sodium on the day following their use. The mechanism of increased sodium excretion was felt to be due to increased urinary concentration of sodium.

Ammonium chloride was also found to increase the sodium excretion when given in doses of 12 gm. per day. Smaller doses produced inconsistent results. However, prolonged therapy with ammonium chloride would not continue to increase the sodium excretion and often a fall of total output would occur with continued administration. When the salt intake was reduced to 2.0 gm. per day, ammonium chloride had no effect on urinary sodium output.

When urea was given in doses of 60 gm. daily there was a transitory increase in urinary volume; however, there was no increase in urinary sodium and no alteration in sodium concentration in the urine.

Patients with toxemia were studied as to water and sodium excretion. It was found that these patients responded similarly to normal pregnant women as regards the dextrose and mercurial diuretics. Eight patients with toxemia were given 10 to 15 gms. of ammonium chloride in 5 per cent dextrose and a satisfactory weight loss, indicating indirectly a loss of water and sodium, was found. Three eclamptic patients had progressed to a point of marked oliguria. Two of these patients had prompt return of urinary flow after an intramuscular injection of $7\frac{1}{2}$ grains of aminophylline.

It has been suggested that morphine has an antidiuretic effect. Twenty patients were given 10 to 15 mgm. of morphine at the onset of an infusion of 5 per cent dextrose. Many of these patients showed a sodium and water retention for 3 to 4 hours following the injection.

It is apparent from this study that so-called diuretic agents have been very loosely defined. Often a transitory effect would be noted in the sodium excretion which would be followed by sodium retention. The action of these agents falls into 3 main categories. The first of these is a "wash out" mechanism which acts by producing an increased sodium excretion by an increased urinary output. A second mechanism of increased sodium excretion is produced by a change in the acid-base balance. The third mechanism by which sodium excretion may be increased is by altering the renal function so that there is an increased urinary sodium concentration. No claims are made by the authors for the use of these agents in toxemia, but it appears that the toxemic patient responds to these drugs in a fashion similar to that of the normal pregnant woman.

THE EFFECTIVENESS OF VARIOUS DIURETIC AGENTS IN CAUSING SODIUM EXCRETION IN PREGNANT WOMEN

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Am. J. Obst. & Gynec., 56: 1-22, 1948

Recently there has been widespread interest in the role of sodium in the production of edema. Because of this interest in sodium and in the factors involved in augmenting its excretion, a series of studies were undertaken by the authors to investigate the effects of so-called diuretic agents on the fluid and sodium excretion in women with normal and toxemic pregnancies.

In this series, the sodium determinations were made by a colorimetric technique based on the original gravimetric method. The patients were carefully controlled concerning diet and fluid intake and output. The dietary sodium was calculated to range from 1 to 1.5 gm. for low salt diet, to 10 to 15 gm. for the high salt diet. Usually 3 days were required for the patient to stabilize on any given diet.

On an average hospital diet of 6 to 8 gm. of sodium chloride, the daily sodium excretion was found to be a parallel figure. If the dietary sodium were suddenly increased, a lag period of several days would ensue before excretion would equal intake.

If fluid intake were increased by 2000 to 4000 cc. per day, a marked increase in urinary output was noted, but concurrently there was a decreased excretion of sodium during the day that fluids were forced. Not only was the concentration of sodium per liter of urine reduced, but the 24-hour sodium output was also diminished. It made little difference if the fluid was given in 2 to 3 hours or over a 24-hour period. When the fluids were given by vein the greatly increased urine volume produced a slight increase in sodium excreted in 24 hours.

To determine the effect of intravenous dextrose on sodium excretion, 200 gm. of dextrose was given in 5, 10, 25 and 50 per cent concentrations as rapidly as clinically feasible. The process was then reversed and the volume was held constant; the patient was given 400 cc. of each concentration. When 200 gm. of dextrose was given as a 50 per cent solution there was a slight diminution of the total sodium excretion, and as the volume of fluid was increased and the concentration decreased there was a progressive increase in the sodium excretion, with 4000 cc. of 5 per cent solution producing a consistent increase in sodium output. However, when the volume was constant no appreciable change was noted in 24-hour excretion of sodium, regardless of concentration. It was concluded that the addition of dextrose to intravenous fluids does not seem to augment the diuretic effect of the water which carries it.

The effect of aminophyllin was studied by administering the drug in doses ranging from 1 grain twice daily to 7½ grains three times daily. The smaller

1945 were compared with those who had had their eclamptic convulsions prior to 1940, it was found that the incidence of post-eclamptic hypertension was less than half as frequent in the more recent group. The length of follow-up was the same for the 2 groups. It was suggested that this reduced incidence of hypertension may have resulted from a more radical management of pre-eclampsia. Previously the pre-eclamptic patient was allowed to continue with her toxemia for periods up to several weeks, whereas now treatment is somewhat more prompt, and prolonged toxemia is avoided. There was no increase in the incidence of hypertension in a 6-year interval among the patients examined both in 1940 and 1946. Five of the 22 living women with hypertensive readings in 1940 had normal pressures in 1946. Three who had been normal in 1940 were hypertensive 6 years later.

One hundred and twenty-five patients in this series had 226 pregnancies subsequent to the eclamptic attack studied. The fetal loss was 20.3 per cent, with 26 abortions (7 therapeutic), 17 stillbirths (14 with maternal toxemia), 2 neonatal deaths and one tubal pregnancy. The recurrence rate of toxemia of some degree was 34 per cent in pregnancies carrying to the period of viability. Forty-five per cent of the women pregnant again had at least one later toxemia.

Although one cannot give a certain prognosis to individual patients, it is possible to assess the probability of recurrence of toxemia if one has certain data concerning the eclamptic pregnancy. The factors which suggest an unfavorable prognosis are: (1) an initial systolic blood pressure at the first visit and before the onset of toxemia above 120 mm. Hg; (2) an average blood pressure, in eclampsia, above 160 mm. Hg; (3) a duration of toxemia of more than one week; (4) failure of the blood pressure and urine to return to normal by the tenth postpartum day; and (5) a weight/height ratio, at follow-up, greater than 2.2 pounds per inch.

(Among students of the toxemias of pregnancy, surely no one in the past decade has made greater contributions than Chesley and here is the report of another meticulous and informative investigation. To single out just one little point in this comprehensive paper, Chesley's quantitative approach to obesity by means of the height-weight ratio might well be put to more general use as a prognostic sign than it now probably enjoys. His idea of course is that the greater the height-weight ratio at follow-up (when the patient asks about another pregnancy) the higher is the incidence of toxemia in later pregnancies. When the weight in pounds divided by the height in inches is less than 2.2, Chesley finds the incidence of recurrence of toxemia to be about 25 per cent; on the other hand, when this ratio is 2.2 or above, the frequency of recurrence soars to over 70 per cent. In other words, obesity is a bad prognostic sign. We have all known this for a long time but this method of quantitating obesity and correlating it with ultimate results, impresses me as a step forward.

Because of the catastrophic picture of convulsions, patients who have suffered them and especially their families, are often loathe to consider subsequent pregnancies. Moreover, the literature in general presents a rather gloomy forecast for these women in later child-bearing, the recurrence rate of toxemia (not necessarily eclampsia) in some series running as high as 80.5 and 94.5 per cent, the average for all recent reports being near 45 per cent. Because of these several circumstances the actual outlook which post-eclamptic women face in subsequent pregnancies assumes great practical importance.

Our results at the Johns Hopkins Hospital have been rather better in post-eclamptic pregnancies than those commonly reported and I am inclined to be rather sanguine about

(This is an important but disillusioning paper since it indicates that the most commonly used diuretic agent in eclampsia, hypertonic glucose solution, is perhaps not as efficacious in ridding the body of water and soda as we have liked to believe. If the objective is to promote the elimination of sodium, it would appear from this study that the "washout mechanism" as produced by 5 per cent solutions of glucose may be more efficacious than the more concentrated preparations.

It may well pan out that the most efficacious means of stimulating excretions of both water and sodium in eclampsia is conduction anesthesia. The report of Hingson, Whitacre and Turner on 74 cases of eclampsia treated in this manner with only 3 maternal deaths is certainly promising, especially since many of these patients were neglected women sent in from the countryside (Lull and Hingson: *Control of Pain in Childbirth*, J. B. Lippincott Co., p. 406). However, as this method of treating eclampsia becomes better known, as it doubtless will, the following word of warning is mandatory: The procedure should never be attempted by anyone other than an expert anesthesiologist or an obstetrician especially trained in its use and aware of the hazards involved. Unless skillfully and judiciously administered, blood pressure drops may be precipitous. In the hands of the average man, including the average specialist, our old stand-bys, sedation, magnesium sulfate and intravenous glucose are unquestionably safer.—Ed.)

A FURTHER FOLLOW-UP STUDY OF ECLAMPSIA

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Am. J. Obst. & Gynec., 56: 409-421, 1948

There have been 245 cases of convulsive eclampsia occurring in 242 women at the Margaret Hague Maternity Hospital from Oct. 16, 1931, through Dec. 31, 1945, with an incidence of 1 in 335 deliveries. Thirty-four of these women are known to be dead and 20 were reexamined in 1946 with special reference to the presence or absence of vascular disease and the outcome of the first and subsequent pregnancies. All but 2 of the eclampsia survivors had been followed for at least a year or until death. In 1940, 141 of these patients were seen at follow-up, and all but 5 of these were rechecked in 1946.

The immediate maternal mortality was 10 per cent and the fetal loss 33 per cent. There were 12 remote deaths, 6 of which were in the cardiovascular field. The remote annual death-rate in the immediate survivors of eclampsia was 6.39 per 1000, or $2\frac{1}{4}$ times the expected rate. There was a higher death-rate in the first two years post eclampsia; however, it was largely coincidental, since most of the deaths were intercurrent.

In reporting the incidence of hypertension, the authors used 140 mm. Hg or greater in the systolic and a pressure of 90 mm. Hg or greater in the diastolic as the base line. It was recognized that at this level certain patients would be included who merely had a labile blood pressure. The incidence of hypertension was 15 per cent. An additional 7 per cent had elevations in either the systolic or diastolic pressure alone. When the patients treated from 1940-

After a hot enema and 4 mms. of Pitocin did not induce labor, the membranes were ruptured and hard regular contractions began, lasting for about six hours. Tucker-McLane forceps extracted a 7 lbs. 3 oz. viable female. The placenta separated well.

During the postpartum period there was a persistent trace of albuminuria and an elevation of blood pressure varying between 178/112 and 140/100. When seen at 4, 6 and 10 weeks and at 5 months and one year, the patient had no complaints and the blood pressure was down to 120/80.

The authors recommend that in the treatment of such cases, the following be instituted; (1) drastic reduction of sodium ion and fat intake, (2) moderately high protein intake, (3) minimum weight gain, (4) adequate sedation, (5) sufficient rest and (6) interruption of pregnancy if toxemia appears. With the proper supervision they feel that it is possible for some of these hypertensive women to attempt pregnancy.

CHILDBEARING IN THE TUBERCULOUS GRAVIDAE

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J. Obst. & Gynaec. Brit. Emp., 55: 624-629, Oct. 1948

During the period, January, 1947 to March, 1948 inclusive, 150 pregnant tuberculous patients were delivered in the maternity unit, Robroyston Hospital, Glasgow. No selection was made in the patients admitted; all were recommended for admission from tuberculosis dispensaries and antenatal clinics, and accordingly results obtained may be regarded as applying to all types of tuberculous lung lesions associated with pregnancy.

Deterioration observed, clinically and radiologically during pregnancy, labor, and for approximately 2 to 3 months following delivery, was attributed to the effects of childbearing on the lung condition. Classification of tuberculous lung lesions being variable, it was decided for practicable purposes, to group patients on admission according to the following scale of assessments:

(1) "Quiescent" cases, in which the general condition of the patient was good; toxemia was absent; tubercle bacilli were not present in the sputum, and serial skiagrams showed no sign of pulmonary progression. This group comprised 73 cases.

(2) "Arrested" cases, in which the disease had been quiescent over a continuous period of 2 years. This group comprised 13 cases.

(3) "Recovered" cases, in which the state of quiescence continued uninterrupted for 5 years. This group comprised 6 cases.

(4) "Active" cases, discharging tubercle bacilli in the sputum during the preceding 3 months. This group comprised 58 cases.

the outlook for these patients provided they have neither hypertension nor proteinuria at the time of the subsequent conception. In 48 post eclamptic pregnancies followed during the past 12 years in our Clinic and in which the prior eclamptic attack was also observed in this institution, the recurrence of some form of toxemia was seen in 25 per cent, but the picture was usually mild. Eclampsia was not repeated. In only 3 of the 37 patients was advanced hypertensive vascular disease present. No fetal loss occurred in patients who went beyond viability and abruptio was never observed. In addition, 84 patients have been studied who were said to have had eclampsia in other institutions. In 245 subsequent pregnancies in this group there were 2 instances in which eclampsia recurred or less than 1 per cent. In pregnancies which went to viability, the fetal loss was 6.4 per cent. There were no maternal deaths in either of these 2 series and the impression we derived from reviewing them is that the likelihood of recurrence of toxemia after eclampsia, including even the mildest examples, is not more than 30 per cent, that the chances of eclampsia repeating itself under good management is less than 1 per cent, that the probability of permanent hypertensive vascular disease resulting is about 10 per cent, while the outlook for a living child is better than 80 per cent. If the patient has no hypertension or proteinuria at the time of the subsequent conception, the outlook for a living child is probably better than 90 per cent. On the other hand, if the same patient has experienced a toxemic pregnancy since the eclampsia, the prognosis for subsequent pregnancies is less good but not altogether discouraging.—Ed.)

PREGNANCY FOLLOWING THE SMITHWICK OPERATION FOR HYPERTENSION

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Am. J. Obst. & Gynec., 56: 805-806, 1948

Because of the few women who have gone through pregnancy following the Smithwick operation for hypertension the report of such a case is instructive. Mrs. B. presented a case of essential malignant hypertension with one pregnancy prior to and one following a Smithwick operation. When she was first seen she was 26 years old, gravida ii, and approximately 3 months pregnant. Past history revealed that the blood pressure had varied between 200 to 250 systolic and 90 to 120 diastolic for a year previous to the Smithwick operation. Following this, the blood pressure dropped to 90 to 120 systolic and 70 to 80 diastolic with renal function normal. One previous pregnancy had been marked by severe nausea and vomiting. A viable male child was delivered.

General physical was negative. Blood pressure was 138/90. The fundus was 8 cms. and pelvimetry showed a gynecoid pelvis. Chest X-ray, urinalysis and Fishburg tests were negative.

A tendency toward excessive weight gain in the fourth month was controlled by the restriction of salt, fluids and diet. A trace of albuminuria was noted in the ninth month, accompanied by a rise in blood pressure to 140/110. Nausea and frontal headaches were also present. This mild toxemia resulted in the hospitalization of the patient for induction of labor.

the pregnancy was performed; clinical status at the end of the observation period is noted.

In February, 1947 special provision was made in the maternity unit and associated antenatal and postnatal clinics, Robroyston Hospital, Glasgow, for the observation and treatment of expectant and nursing tuberculous mothers, all of whom, resident within the city, were eligible for admission. In order that contingencies of an obstetrical and medical nature might be investigated and treated simultaneously, the staff included a consultant obstetrician and a chest physician, while the responsibility for the infant after delivery and during the neonatal period devolved upon the pediatrician to the hospital. Breast feeding, except in certain selected cases, was forbidden.

In the patients under review prior consideration was given to the lung lesion, the pregnancy being regarded as secondary in significance. Where indicated, surgical procedures designed to secure partial and complete immobilization of the diseased lung were applied, not only during the pregnancy however long its duration, but throughout the puerperium.

Where pregnancy was advanced less than 5 months, therapeutic interruption was performed if the case was one of advanced pulmonary tuberculosis in which collapse therapy was contraindicated. Later than this period pregnancy was allowed to proceed to term and, where possible, labor was shortened and dystocia avoided. Spinal anesthesia was preferred to inhalent drugs. On discharge from the hospital advice was given the mother regarding contraception, and she was advised to report, with her child, to the postnatal clinic in 3 months' time for further assessment.

While the authors' figures are statistically insignificant to justify final pronouncements on the precise influence of age and parity on the evolution of pulmonary tuberculosis, the impression was formed that, generally, primiparae fared better than multiparae, presumably because the health of the latter had become impaired by repeated pregnancies and domestic responsibilities, resulting in lowering of the powers of resistance to a dangerous level. It is interesting to note that while Jameson (Jameson, E. M. (1935): *Gynecological and Obstetrical Tuberculosis*. Philadelphia, Lea and Febiger) supports this view, Cohen (Brit. J. Tuberc., 40: 10, 1946) disagrees.

Although ceding the point that pregnancy may have an adverse effect on tuberculous lung lesions, results obtained in this investigation tend to show that therapeutic interruption does not necessarily bring about an improvement in the phthisical condition. In conclusion the writers are of the opinion that collapse therapy is the sheet anchor for gravidae with active tuberculosis.

Table II is an attempt to correlate age and parity distribution with the clinical status of the patient at the end of the period of observation.

Tuberculosis antedated the pregnancy in 108 patients; in 11 of whom the operation of thoracoplasty had been carried out prior to admission, while in 10 others, artificial pneumothorax was maintained concurrently with the pregnancy. The remaining 87 patients gave a history of routine sanatorium treatment, with artificial pneumothorax in 53, and phrenic nerve interruption in 10. Four deaths were recorded in this group of patients.

TABLE II

AGE GROUP (YEARS)	PRIMIPARAE				MULTIPARAE				TOTAL
	Imp.	ISQ	Worse	Dead	Imp.	ISQ	Worse	Dead	
19-23	6	16	1	2	2	5	3	0	35
24-28	5	25	4	3	4	17	4	3	65
29-33	2	8	0	2	5	11	2	4	34
34-38	0	4	0	1	1	7	0	1	14
Over 39	0	0	0	0	1	1	0	0	2
Total.....	13	53	5	8	13	41	9	8	150

TABLE IV

METHOD OF TERMINATION	PRIMIPARAE					MULTIPARAE				
	Imp.	ISQ	Worse	Dead	Total	Imp.	ISQ	Worse	Dead	Total
Surgical induction....	0	0	0	0	0	0	0	0	1	1
D & C.....	0	0	0	0	0	0	0	0	1	1
Hysterotomy and sterilization.....	1	0	3	2	6	1	0	1	0	2
Hysterotomy without sterilization.....	1	1	1	0	3	0	0	0	0	0
Cesarean section.....	0	0	0	0	0	0	1	0	0	1
Total.....	2	1	4	2	9	1	1	1	2	5

Collapse-therapeutic measures in their many forms were applied with success to 20 patients during gestation: 12 had artificial pneumothorax induced, with section of adhesions in 7; 1 patient, $3\frac{1}{2}$ months pregnant on admission, was the subject a of 2-stage thoracoplasty operation.

Dyspnea of moderate degree was noticed in 18 patients during the height of the second stage of labor, and of these 2 had received thoracoplasty operations and 8 artificial pneumothorax treatment, while the remaining 8 patients suffered from advanced pulmonary tuberculosis.

Two multiparae, seen for the first time at the 6th month approximately, died undelivered; in both the lung lesion was advanced and bilateral and in 1, tuberculous meningitis complicated the condition.

No deaths occurred during labor.

Table IV shows the number of patients on whom therapeutic interruption of

its peak between 7 and 8 pounds, and rapidly falls off so that at a weight of 10 pounds only about 2 per cent of the group are included. The distribution curve for the children of the 100 prediabetic mothers (Group 1) is displaced toward the higher weights. Although the peak in this group also occurs between 7 and 8 pounds, the percentage of babies in the higher weight groups is considerably greater than in the controls.

The average birthweight of children born to the prediabetic mothers was 8.9 pounds or 4.0 kilograms, whereas the average birthweight of the children of the control mothers (Group 2) was 8.0 pounds or 3.5 kilograms. Statistical analysis of the birthweight data shows that the standard error of the difference between the means of Groups 1 and 2 is 0.144 pounds. Calculated on the basis of probability, a difference of 0.9 pounds between means is statistically significant. The authors data are, therefore, in agreement with those of Miller (New England J. Med. 233: 376-378 (Sept. 27), 1945) in demonstrating that the average birthweight of children born to prediabetic mothers is greater than that of children born to normal mothers.

In the 58 of the 100 prediabetic patients who gave birth to big babies, the average age at the time of birth of the first big baby was 22.9 years. Diabetes was diagnosed at an average age of 47.1 years, and the "latent period" between the birth of the big baby and the development of clinical diabetes averaged 24.2 years. In this series the shortest latent period was 1 year and the longest was 46 years. Only 5 of the 58 patients had a latent period less than 10 years.

On the basis of the authors' data, a table has been constructed permitting rough estimation of the accuracy with which one may predict the subsequent development of diabetes in a woman giving birth to a baby having a specified weight in excess of 10 pounds. It shows that as the birthweight of the baby rises, the prediction accuracy increases progressively and is about 25 per cent when the baby weighs more than 10 pounds, about 50 per cent when it weighs more than 11 pounds and exceeds 60 per cent when the infant weight is more than 13 pounds.

PRIMARY ABDOMINAL PREGNANCY IN THE LESSER PERITONEAL CAVITY

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West. J. Surg., 56: 410-413, 1948

The author discusses the two general types of abdominal pregnancy, namely, primary and secondary—so called because of the assumed mode of implantation and development. The usual secondary abdominal pregnancy develops from a

THE RELATION BETWEEN INFANT BIRTHWEIGHT AND SUBSEQUENT DEVELOPMENT OF MATERNAL DIABETES MELLITUS

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J. Clin. Endocrinol. 8: 380-389, May, 1948

That diabetic women frequently give birth to unusually large infants is well known. Only recently, however, has it been emphasized that infants of excessive weight may be born to mothers before clinically apparent maternal diabetes mellitus develops (Am. J. Obst. & Gynec. 38: 982-992 (Dec.) 1939). Thus, the average weight of infants born to prediabetic mothers considerably exceeds the normal (New England J. Med. 233: 376-378 (Sept. 27), 1945). The combined fetal and neonatal mortality rate is high in the prediabetic group as well as in the diabetic (J. A. M. A. 124: 271-275 (Jan. 29) 1944), and similar fetal, visceral changes are present in both groups (Am. J. M. Sci. 209: 447-455 (April) 1945). This study was undertaken to ascertain how the birthweight of an unusually large baby can be correlated with the likelihood of the subsequent development of maternal diabetes, and to determine the average time elapsing between the birth of a large baby and the development of clinical diabetes.

One hundred parous, diabetic women with an average age of 55.3 years, who remembered the birthweights of their children, constitute the diabetic group (Group 1). These individuals were outpatients of the Washington University Diabetic Clinic or were hospitalized on the medical service of the Barnes Hospital. An equal number of parous women without glycosuria or symptoms of diabetes, from the medical and surgical public wards, served as controls (Group 2). The controls were also largely beyond the childbearing age; their average age was 51.2 years.

Three hundred and sixty children were born to the 100 prediabetic mothers, and 315 were born to the control women of Group 2. A striking correlation between the birth of big babies and the prediabetic state is shown. Of the 144 infants in these 2 combined series, weighing 10 pounds or more, 77.1 per cent were born to women destined to develop diabetes. Compared to the control series, the preponderance of large infants coming from prediabetic women increased as the birthweight rose. For example, 87.2 per cent of babies weighing 11 pounds or more were born to prediabetics, and only 7.7 per cent were born to normal women from a nondiabetic family. At the level of a birthweight of 13 pounds or greater, 23 of 24 infants, or 95.8 per cent, came from prediabetic mothers.

The extent to which the prediabetic state influences the birthweight of the infant is shown in an informative distribution curve. The distribution curve of infant birthweights from the 100 mothers of the control group (Group 2) has

BILATERAL TUBAL GESTATION

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Brit. M. J., 1: 734, 1948

Bilateral tubal gestation is rare, and until 1942 only 80 cases had been described in the literature.

The author presents the case of a 30-year-old Arab woman who had 2 children, aged 10 and 4 years. She had had several hospital admissions following the birth of the last child because of lower abdominal pain, and was found to have gonococcal cervicitis and salpingitis. Her last admission had been 8 weeks prior to her present illness. She returned complaining of left-sided abdominal pain and vaginal discharge and, in addition, stated that she had missed two menstrual periods.

Examination on admission revealed tenderness in the left iliac fossa. Vaginal examination showed a slight bloody discharge, normal uterus and cervix, and a tender, rather indefinite swelling connected with the left tube. A tentative diagnosis of salpingitis was made and she was treated in the usual manner. Four days later she had an attack of severe right lower abdominal pain with a rise in pulse rate, abdominal distention and tenderness and fullness in the right fornix. She was again treated conservatively for 14 days, when the swelling on the left side was found to be more definite and there was a mass in the left iliac fossa. The uterus was raised and displaced to the left, and there was a semi-cystic swelling in the right fornix extending up into the right iliac fossa.

Laparotomy was performed and a typical tubal pregnancy was found in the distal half of the left tube. On the right, there was a large walled-off hematoma, and the distal end of the right tube was eroded for a distance of one inch. Section of the right tube revealed chorionic tissue; however, embryonic remains could not be found in the clot.

The question as to whether the fetuses could have been simultaneously viable cannot be answered in the absence of embryonic remains. However, it is probable that the fetus in the right tube was younger than that on the left.

CHRONIC ULCERATIVE COLITIS AND PREGNANCY

J. FELSEN AND W. WOLARSKY

New York, N. Y.

Am. J. Obst. & Gynec., 56: 751-755, 1948

An analysis is made of 34 women with chronic ulcerative colitis during 50 pregnancies. There were 43 full term deliveries, 3 miscarriages, 2 therapeutic abortions, one tubal pregnancy and one induction of labor at 6 months.

tubal gestation as the enlarging placenta spreads from its primary site within the wall of the tube, through the wall, and out through the fimbriated end of the tube onto adjacent pelvic structures. The type referred to as secondary presumably develops by implantation of the fertilized ovum in the fallopian tube. Complete extrusion of the fetus and placenta by tubal abortion or rupture and reimplantation of the conceptus elsewhere occurs. In primary abdominal pregnancy, the fertilized ovum presumably implants itself on the peritoneal surface without previous implantation in the tube, ovary or uterus.

Abdominal pregnancy is rare, occurring about once in 2,300 deliveries. By far the most common type is the secondary pregnancy. However, proved primary pregnancies have been reported under the serosal surface of the uterus, the tube, the broad ligament, the cul-de-sac or rectum, the mesosigmoid, recto-sigmoid, omentum and lumbar gutter. A few cases have been described with implantation as far removed as the right lumbar gutter, the liver, the spleen and, in the case under discussion, in the lesser peritoneal sac.

In this case the patient was a 29-year-old colored woman, gravida V, para III. She was admitted to the San Francisco Hospital 3 months after her last period with the complaint of left mid-abdominal pain radiating to the left flank and back. On examination the uterus was found enlarged to twice its normal size. It was soft and symmetrical and there were no adnexal masses. There was a tender mass in the left upper quadrant measuring about 8 cm. in diameter. X-ray revealed a $3\frac{1}{2}$ to 4 month fetus in the left upper quadrant. On operation, immediately anterior to the left kidney, posterior to the stomach, lateral to the vertebral bodies and within the lesser peritoneal sac an 8 cm. living fetus was found. Moderately severe bleeding was encountered during exploration of the area and so the cavity was packed with oxycel and left otherwise undisturbed. The postoperative course was stormy but the patient recovered, the only residuum being a persistent left upper quadrant mass.

The author feels that the location in the lesser peritoneal cavity near the left kidney would seem to make this a most convincing example of primary abdominal implantation. The route of the fertilized ovum is open to speculation but the most likely probability is that it perforated the mesocolon by trophoblastic activity. Direct evidence against the theory of reimplantation following tubal abortion was lacking, but it is doubtful that a fetus of this size could remain viable during the period of transmission and reimplantation.

Two months after the initial examination, the patient developed a severe constant pain in the right lower quadrant which radiated medially toward the pubis. This was accompanied by slight nausea. Pelvic examination showed an enlarged uterus and also a questionable mass in the right lower quadrant. X-ray of the pelvis demonstrated a 4-month fetal skeleton. There was also an area of increased density in the right mid-abdomen which extended from about 2 inches above to possibly $2\frac{1}{2}$ inches below the crest of the ileum. The lower part of the mass appeared to contain teeth and other bony structures. In the left mid-abdomen there was a smaller dense shadow which appeared similar to the shadow on the right.

The pain on the right side persisted and it was felt that torsion of the tumor pedicle had occurred on that side. Laparotomy revealed a moderate amount of cloudy free fluid in the abdomen. The dermoid cyst of the right ovary was 9 cm. in diameter and was hemorrhagic in appearance with moderate torsion of the pedicle. The left dermoid cyst was 8 cm. in diameter, nonadherent and with no visible normal ovarian tissue. A bilateral oophorectomy and right salpingectomy were performed. Pathological examination showed bilateral dermoid cysts with a large corpus luteum on the right and hemorrhagic infarct of the right tube and ovary.

The postoperative course was essentially uneventful. The patient was given large doses of progesterone although at no time was there any evidence of a threatened abortion. She delivered a living female child at term and the postpartum course was uneventful.

The writer believes that certain complications of dermoid cysts make it imperative to remove these tumors during pregnancy. The changes which make surgery necessary are: possible malignant changes during pregnancy, torsion of the pedicle of the cyst, suppuration of the tumor, hemorrhage into the cyst, rupture of the dermoids with chemical peritonitis, mechanical interference with labor, malpresentation and uterine inertia. Operation should, if possible, be delayed until after the ninetieth day of gestation. In the absence of the above complications labor is probably managed most satisfactorily by cesarean section with removal of the cyst being carried out at that time. Though the need for progesterone therapy following operation is not imperative, it is a valuable adjunct to postoperative care at any stage of pregnancy.

Classification of the disease was based on the severity of symptoms and the bowel pathology seen at sigmoidoscopy. A table giving the severity of symptoms is included. The authors point out that the diagnostic value of the sigmoidoscope is great, and feel that with gentle manipulation and with the patient in the left Sims' position it can be used with benefit until the sixth month of gestation. Proctoscopy can be instituted at any time during pregnancy.

All of the full term pregnancies ended in live births. There appeared no causal relationship between the three miscarriages and the disease. None of the 34 women suffered any lasting effects or encountered any major obstetrical difficulties. One patient with severe ulcerative colitis has been free of the disease for four years following the birth of the third child.

In 13 cases, or 30% of the pregnancies, the colitis was somewhat aggravated in the first trimester. The colitis was definitely ameliorated in 58% of the pregnancies and unchanged in 12%. The authors conclude that ulcerative colitis is not an indication for interruption of pregnancy in 70% of the women with the disease. That pregnancy should be associated with improvement of the disease is hard to explain. Increased rest and better care were given to a nonpregnant group also, but they failed to respond as well. Perhaps the enhancement of protective antibodies during pregnancy is responsible.

(This report covers an unusually large experience with ulcerative colitis in pregnancy and should serve as a valuable guide to obstetricians who occasionally encounter this complication. In cases of this disease which become worse in gestation, the causative factor may be of a psychogenic nature rather than any direct effect of the pregnancy itself. Thus, the case of ulcerative colitis in gestation with which we have had the greatest difficulty was one in which there were repeated marital squabbles after every one of which the patient experienced an exacerbation of diarrhea and had to be admitted to the hospital. Fear on the part of the patient that pregnancy will aggravate her disease may likewise precipitate an exacerbation. Hence, reassurance is a most important part of the management of these cases.—Ed.)

BILATERAL OVARIAN DERMOID CYSTS COMPLICATING PREGNANCY

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Ohio State M. J., 44: 819-820, 1948

The case is presented of a 33-year-old female who was first seen because of nausea, vomiting and absence of menstruation for 2 months. She had delivered one normal male child 10 years previously, and had had one spontaneous abortion about 6 months prior to this visit. The menstrual history was otherwise entirely negative. Pelvic examination showed a uterus the size of a 6 weeks' pregnancy.

Two months after the initial examination, the patient developed a severe constant pain in the right lower quadrant which radiated medially toward the pubis. This was accompanied by slight nausea. Pelvic examination showed an enlarged uterus and also a questionable mass in the right lower quadrant. X-ray of the pelvis demonstrated a 4-month fetal skeleton. There was also an area of increased density in the right mid-abdomen which extended from about 2 inches above to possibly $2\frac{1}{2}$ inches below the crest of the ileum. The lower part of the mass appeared to contain teeth and other bony structures. In the left mid-abdomen there was a smaller dense shadow which appeared similar to the shadow on the right.

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CHOREIFORM BEHAVIOR DURING PREGNANCY WITH DATA ON FIVE CASES

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Proc. Staff Meet., Mayo Clin., 23: 382-384, 1948

Pregnancy complicated by chorea, chorea gravidarum or, as it perhaps should be called, "choreiform behavior during pregnancy," is an infrequent complication of the gravid state; however, it presents a grave and distressing problem. Analysis of the 5 cases of chorea gravidarum treated at the Mayo Clinic showed that the average age was 21 years. Four of the patients were married and one was not. Three of the patients were multigravidas and 2 were primigravidas. In all of the cases chorea began in the first half of pregnancy and lasted for periods varying from $2\frac{1}{2}$ weeks to 5 months. All of the pregnancies terminated spontaneously at term and 6 normal babies were born (one set of twins). No evidence to support toxemia as an etiologic factor was present in this series. A rheumatic background was present in all of the cases. Heart disease existed in 3 cases. Psychogenic color was present in 4 cases.

The authors believe that though this is a serious complication of pregnancy, the prognosis for mother and child is good. Although there is a school which feels that this disease is a separate pathologic entity, probably dependent on the pregnancy, the writers think that it is merely Sydenham's chorea occurring during pregnancy. Some authors have stressed the psychogenic factor in an etiologic role and it is true that the incidence of chorea is higher in illegitimate pregnancies. However, it seems more likely that the psychogenic factor acts in a precipitating rather than in a causative manner. Rheumatic fever is undoubtedly associated with this condition, and about one-third of the reported cases show evidence of heart disease. Treatment of choreiform behavior during pregnancy is conservative and it rarely becomes necessary to interrupt pregnancy.

(The old idea that there is some special form of chorea peculiar to pregnancy, so called "chorea gravidarum," crops up every now and then. Hence it is worthwhile recalling, as the authors do, that there is actually no such entity and that all such cases are simply examples of Sydenham's chorea which happen to occur in gestation. While it is conceivable that psychogenic factors brought into play by pregnancy may conceivably precipitate the disease, this appears unlikely, because, if so, chorea in pregnancy would be much more common than it is. Thus, Burr, writing from the viewpoint of a neurologist, states: "St. Vitus Dance is the most frequent acute nervous disease of childhood. It is more frequent even than epilepsy. If the danger of a recurrence in pregnancy were very great, the number of cases of chorea would be very large; really it is small." (*Am. J. Obst. & Gynec.* 17: 653, 1929.)

It is informative to note that in all 5 of these Mayo Clinic cases, a rheumatic background was demonstrable and that outright heart disease existed in 3. In the classic study of chorea in pregnancy by Willson and Preece, surveying 951 cases in the literature which occurred in 797 women, they found that more than 50 per cent of the gravidae gave a history

of having had a previous attack of chorea; more than one-third had had rheumatism and more than one-fourth had had both rheumatism and chorea (Arch. Int. Med. 49: 471, 1932). Fraipont has reported 50 autopsies in which valvular lesions were found in 66 per cent (Quoted by Campbell; Am. J. Obst. & Gynec. 16: 881, 1928). These data serve to emphasize the fact that if cases are studied diligently enough, a rheumatic background will be found in almost all, valvular disease in the majority. This is why fever is such a grave prognostic sign in these patients since it indicates that active damage is being done to the heart muscle and valves. Most cases of chorea in pregnancy do very well under simple medicinal treatment, but the febrile patients do extremely badly no matter what is done. For instance, in 34,569 pregnancies observed by Stander at the New York Lying-in Hospital, 12 patients were considered to have chorea; 11 went through pregnancy without appreciable difficulty but 1 died from subacute bacterial endocarditis.—Ed.)

RETREATMENT OF THE PREGNANT WOMAN FOR SYPHILIS FOLLOWING PENICILLIN

IS ADDITIONAL THERAPY NECESSARY WHEN EFFECTIVE TREATMENT HAS BEEN
GIVEN PRIOR TO CONCEPTION?

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WITH

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Am. J. Obst. & Gynec., 56: 340-346, 1948

This is a study of 52 mothers treated with penicillin for syphilis before, but not during, pregnancy. There were 46 normal cases with a normal outcome and no syphilitic infants resulted. There were 3 abortions, one miscarriage, one stillbirth and one neonatal death, but none of these could be attributed directly to syphilis and they probably resulted from other causes.

The following criteria were established for the selection of cases in whom retreatment for syphilis was considered unnecessary: (1) The woman was previously treated for symptomatic early syphilis and had a normal clinical and serological response. (2) The woman was treated for latent syphilis and showed no evidence of progression of her disease. (3) The woman was treated for symptomatic late syphilis and sustained a normal response, depending upon the type of disease present. However, there may be a possible fallacy in basing judgment solely on the clinical response, and this factor must not be overlooked.

So far as could be determined from this limited series of cases, retreatment for syphilis during pregnancy is unnecessary, provided the expectant mother's response to previous penicillin therapy has been normal and reinfection has not occurred. However, the great effectiveness and relative safety of penicillin to

prevent congenital syphilis makes retreatment of the pregnant woman desirable if there is any doubt whatever of the effectiveness of her previous antisyphilitic therapy.

RUPTURE OF CORPUS LUTEUM OF PREGNANCY DURING COITUS CAUSING ACUTE ABDOMEN FOLLOWED BY ABORTION

W. R. SLOAN

Brit. M. J., 2: 26-27, 1948

The case is reported of a 33-year-old nurse who was first seen at 11 a.m. on July 20, 1947. Eight hours previously, during coitus, she had been seized with severe lower abdominal pain and nausea. The patient had had one child by cesarean section in 1946. She did not believe herself pregnant at the present time, although her menstrual period was 7 to 12 days overdue. She admitted occasional vague uneasiness in the left groin during the previous week.

The pulse rate was 80; temperature 96 degrees F. The lower abdomen was diffusely and acutely tender—rather more so on the right side. Movement of the cervix caused severe pain. Examination under anesthesia revealed nothing definite, but an impression was received of a vague soft swelling in the left fornix.

On opening the abdomen, a moderate amount of free blood was found in the pelvis. The uterus appeared normal. The left ovary contained a ruptured follicle about the size of a marble. A blood clot was adherent to this. Immediately adjacent was a dark swelling which, on being pricked, showed the yellow convolutions of a recent corpus luteum. The other ovary was normal. The clot was removed and the abdomen closed.

A urine specimen was taken the following day for an Aschheim-Zondek test; this was later reported weakly positive. On the third day a painless period began which lasted for 4 days. Following the period, a slight brownish discharge persisted and curettage was finally performed. Fragments of an early ovum were found in the process of extrusion. Histologic examination confirmed the presence of chorionic villi.

The author considers it likely, though not necessarily conclusive, that the abortion was attributable to impairment of the integrity of the corpus luteum from traumatic rupture.

PATHOLOGY OF LABOR AND PUERPERIUM

FACE PRESENTATION

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Am. J. Obst. & Gynec., 56: 86-99, 1948

This study concerns the results obtained in 160 cases of face presentation occurring at Charity Hospital of Louisiana during the 25 years ending with December, 1946. The incidence of face presentation was 0.184 per cent of 88,114 deliveries.

The condition was found 3 times as frequently in multiparas as in primiparas, the ratio being 119 to 41. It was more common in primiparas in the age group under 20 years and in the multiparous age group of 21 to 30 years. The most common positions were the left and right mentoanterior positions, with mento-transverse and mentoposterior occurring in only about 25 per cent of the cases.

The findings concerning etiology of face presentation were contrary to previous reports. Contracted pelvis or a large baby was responsible in 6 and 8 cases, respectively, whereas parity was a major factor in 52 cases. Nine cases were due to anencephalic monsters, 18 cases occurred with small babies, and in 56 cases the etiology was entirely unexplained. In other instances such factors as hydramnios, cord about the neck, uterine tumors, marginal placenta previa, etc., seemed to play a role.

In 27 cases dilatation of the cervix was delayed or obtained by operative means. Of these, 15 per cent were mentoanterior, 20 per cent were mentoposterior, 21 per cent were mentotransverse, and in 3 cases the position was not stated. It appears, therefore, that the fetal position had little effect on the ease with which cervical dilatation was obtained.

Of the 160 cases, 86 delivered spontaneously, 73 being multiparas and 13 primiparas. The maternal mortality was 0 per cent. The corrected infant mortality was 14.3 per cent. Low forceps were employed in 16 cases with an infant mortality of 12.5 per cent and a maternal mortality of 0 per cent. Flexion of the head was done in 15 cases with no maternal mortality. However, in the 5 cases in which high forceps were used, the infant mortality was 40 per cent, while in other methods the infant mortality was 0 per cent. Version and breech extraction were employed in 27 instances with an infant mortality of 53.3 per cent and a maternal mortality of 3.5 per cent. The one death occurred in a primipara who died of sepsis 25 days after delivery. The duration of labor was a major factor in infant mortality, the death rate increasing with the lengthening of time between rupture of the membranes and delivery. Cesarean section was used in 8 cases with no maternal or infant mortality. Manual rotation followed by

low forceps was used in one case with success. Craniotomy was employed in 3 multiparas with 100 per cent infant mortality and 33 per cent maternal mortality; the one death was due to peritonitis.

Concerning maternal morbidity, it was felt that the more complicated the operation, the higher the incidence of morbidity, so that almost 50 per cent of those having versions and extractions and high forceps following flexion were morbid, while less than 20 per cent of spontaneous deliveries for both primiparas and multiparas resulted in temperature elevation.

Several factors were found to be outstanding in the management of these cases. Early diagnosis is important so that anticipatory measures may be taken. Labor should be conducted guardedly and aseptically, for many patients with face presentation are potential candidates for cesarean section. Since spontaneous delivery does occur in all positions, it should be expected if there is no disproportion, but interference should always be kept in mind as a possibility for safe termination of labor. Version and extraction should have no place in the delivery of face presentations. Cesarean section seems to be definitely indicated in certain selected cases and probably will find more generalized usage.

(In the first paragraph of Reddock's original paper he rightly calls attention to the dearth of studies on face presentation in the American literature. This lapse has been corrected in large measure during the present decade by 3 important articles covering all aspects of face presentation; 1 by Posner and Buch, Surg., Gynec. & Obst. 77: 618, 1943; another by Stephen J. Rudolph, Am. J. Obst. & Gynec. 54: 987, 1947, and the above report by Reddock. To these may be added Mussio and Walker's study of the most troublesome aspect of this complication, namely, the management of posterior face positions (Am. J. Obst. & Gynec. 41: 90, 1941).

The data of the 3 general studies mentioned are in close agreement in showing that face presentation is not as common as usually reported, the respective incidence in these series being: 1:529 deliveries; 1:576; and 1:543. They also show a surprising similarity in the frequency of the posterior variety: Posner and Buch, 26.7 per cent; Rudolph, 32.1 per cent; and Reddock, 25.0 per cent. Unpublished data collected a few years ago on 110 cases of face presentation observed at the Johns Hopkins Hospital revealed that the chin was posterior when the diagnosis was first made in 29 instances or in 26.4 per cent. The practical importance of these figures is this: The really troublesome variety of face presentation, the posterior type, is encountered only once in about 2000 cases, that is, not often enough for any obstetrician to be able to compare personally the relative merits of the various methods of handling it and thereby gain a conclusive experience. Hence, a study of reports such as the ones cited is essential if we are to have a rational basis for the management of this condition. Even the data from these large clinics, when broken down into homogeneous entities, entail a large sampling error and accordingly, conclusions which are at all valid can only be reached by a sort of summation of these reports, especially when the findings in one contradict those of another.

The most striking contradiction in these several reports has to do with a factor which, in my opinion, is perhaps the most important issue in this whole problem, namely the incidence of and the role played by *pelvic contraction*. In Reddock's large series of 160 cases, contracted pelvis was found to be the chief etiological factor in only 6 instances, while a large baby accounted for disproportion in 8 more, making a total of only 14 cases, or 8.8 per cent, in which disproportion loomed large in the picture. As Reddock avows, this is contrary to all past experience. In Posner and Buch's series of 87 faces and 13 brows, there were 29 cases of at least borderline disproportion, that is either pelvic contraction or a child over 8½ pounds. Of Rudolph's primiparous patients, there were 11, or 38 per cent

with some form of pelvic abnormality, while of the 32 multiparous women there were 7, or 22 per cent, with pelvic contraction. Almost half his cases showed either a small pelvis by measurements or an average pelvis with an oversized infant.

Our Johns Hopkins series is in keeping with the findings of the latter authors. The diagonal conjugate measurement in 110 patients was taken in all but 9, and was always checked by an experienced staff member. In these 101 measured pelves, the diagonal conjugate was 11.5 or less in 34, and was 9.75 cm. or less in 13. In the 40 primigravidae of the series in which measurements were recorded, it was 11.5 cm. or less in 19, or about $\frac{1}{2}$; while in 5, or 12.5 per cent, it was 9.75 cm. or less. These figures coupled with those of Posner and Buch, and of Rudolph, can leave little doubt in my mind that the older writers were correct in maintaining that pelvic contraction is a frequent etiological factor in face presentations.

But the great importance of pelvic contraction in this complication lies not in whatever causative role it might play, but in the practical management of these cases. By and large, if the pelvis is ample in dimensions and the infant of average size or smaller, the face case does well whether the chin is anterior or posterior; contrariwise, if the pelvis is contracted, it does badly and attempts to deliver the patient vaginally, whether by correcting the malpresentation or by version and extraction, usually lead to disaster. This is well brought out by our series of 40 primiparae with face presentation on whom pelvic dimensions are available. In 21 cases with normal pelves, 2 babies were anencephalic and died; 1 succumbed in utero before the onset of labor in an eclamptic mother; and a 4th weighing 2000 grams died neonatally. Even if we correct only for the 2 monsters, the fetal mortality rate is less than 10 per cent, and if we correct also for the case of eclampsia, it becomes slightly under 5 per cent. Contrariwise, in the 19 primigravidae with contracted pelves, there were 6 fetal losses, none of which was amenable to correction, giving a fetal mortality of 32 per cent. Turning back to the group of 110 face cases as a whole, the fetal mortality corrected for 5 monsters, was 15.5 per cent; but in the 34 cases of contracted pelvis, it was 29.1 per cent despite 5 cesarean sections; and in 13 cases with a diagonal conjugate of 9.75 cm. or less it was 38.4 per cent despite 3 abdominal deliveries.

Since the above series of Hopkins cases goes back to the beginning of the century, only a small minority of the clinical measurements have had the advantages of confirmation and amplification by x-ray pelvimetry. Mussio and Walker, however, call attention to 3 small android pelves in their 8 posterior face cases and it is quite possible that x-ray evaluation of pelvic architecture in face cases will provide further evidence in regard to pelvic sources of difficulty.

In regard to Reddock's statement that version and extraction has no place in this complication, this is in keeping with the general trend, altogether justified, of employing this operation less and less. His condemnation of the procedure, however, seems to me a little too sweeping. Our experience with version and extraction in face cases is limited to 12 operations performed in the series mentioned above. There were only 2 fetal losses in this group; in 1 of these the diagonal conjugate was 10.5 cm. and in the other it was 11.5 cm. with a 4220 gram infant. Here again, accordingly, the question of pelvic contraction comes up. In its presence, version and extraction is a brutal operation both to mother and infant unless the latter is quite small. However, given a multipara with an ample pelvis, full dilatation and membranes intact or only recently ruptured, plus a posterior face which does not rotate, version and extraction is preferable, in my opinion, to conversion or forceps rotation. But even here, it may be unnecessary since with an ample pelvis these posterior faces usually do rotate if given a little time.

It is not the intention of these remarks to imply that pelvic contraction is the explanation of all dystocia in face cases. But it is one of the first things to think of. All the authors quoted above agree that cesarean section should be used more extensively in this complication. The main place for it is in these cases of actual pelvic contraction. If only they can be screened off for abdominal delivery the remaining patients with normal pelves will usually deliver healthy infants per vaginam without difficulty; and the end result

would be, I should think, a reduction in fetal mortality by one-half. But let it be remembered that face presentations carry a 5 per cent incidence of fetal malformations, especially anencephalus; hence roentgen studies are mandatory before section to rule this out. Actually, as has been indicated, they should be routine in all face cases not only for this purpose but to secure an accurate picture of pelvic size and morphology.—Ed.)

AMNIOTIC FLUID EMBOLISM: REPORT OF A FATAL CASE

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Arch. Path., 45: 366-370, 1948

The authors report the case of a 30-year-old primipara whose pregnancy had been uneventful and whose labor started spontaneously. Upon admission to the hospital the membranes were intact and her general condition was quite satisfactory. She received vitamin K, demerol and seconal, and 2 hours after admission the membranes had ruptured and the caput was presenting. The patient climbed onto a stretcher by herself to be taken to the case room and then suddenly became cyanotic and dyspneic. Despite all measures she died 15 minutes later.

On gross examination very little of significance could be demonstrated in either the mother or the fetus. The cervix was completely effaced and its inner surface abraded in the region where the membranes had ruptured. On microscopic examination of the lungs, all sections revealed throughout most of the pulmonary arterioles and capillaries a varying quantity of the constituents of amniotic fluid. Epithelial squamæ were the dominant member. Many of these embolic foreign squamæ were entangled with, or boxed in by, gatherings of neutrophilic polymorphonuclear leukocytes. Mucin, which had trapped many leukocytes, was present in the larger arterial vessels. Sudanophilic granules and droplets were demonstrated in the capillaries. Lanugo hair was not found. The pulmonary veins were relatively bloodless, while the arterial pathways were congested. Microscopic examination of the heart also revealed the presence of occasional basophilic embolic squamæ in the capillaries and arterioles. Sections of the uterus in the abraded area showed intraluminal epithelial squamæ and mucin in the uterine sinusoids. Sections of other organs were not remarkable.

It was felt that the amniotic contents entered the uterine venous pathways through the abraded area in the lower segment. The sudden death was due to the intravascular entrance of these foreign elements resulting in embolization of the lungs and heart, or a fatal anaphylactoid reaction. The histopathological examination showed that the dominant embolic elements were the basophilic epithelial squamæ, acidophilic granular debris of vernix caseosa origin, and mucin.

(This appears to be a clear-cut example of this accident well presented. Little by little the number of authentic cases such as this are being augmented and before long someone

will be able to review a substantial series. It is one of the few really new concepts to be introduced into obstetrics in recent times and was discussed in extenso in an editorial note in the February, 1948 issue of the Survey, pp. 35-37.—Ed.)

THE OUTCOME OF PREGNANCY FOLLOWING VAGINAL OPERATIONS

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Am. J. Obst. & Gynec., 56: 291-299, 1948

This study was undertaken to formulate a plan for the treatment of vaginal lesions during the reproductive years. Three hundred and ninety patients in whom vaginal surgery had been performed and who subsequently became pregnant were studied.

Two hundred and two patients had major vaginal operations prior to pregnancy and 188 had minor operations. The minor operations had no effect on subsequent pregnancies and labors, nor did labor have any effect on the operative result. The major operations had 2 chief effects on labor. In 3.5 per cent of these cases, delayed descent of the fetal head occurred because of vaginal scar tissue. Delivery by cesarean section was necessary in 8.5 per cent of the patients following major operations, an incidence which is $2\frac{1}{2}$ times as great as normal. Labor affected the operative result adversely in some of this group. There was a 16 per cent recurrence of the condition for which the operation had been carried out and secondary operations were necessary in 3 per cent following delivery.

When symptoms or signs warrant it, minor or major operations may be performed on women of the childbearing age. It is not necessary to urge that childbearing be completed prior to operation, as such operations are compatible with future pregnancies. The fact that a pregnant patient has had a major vaginal operation is never an indication to terminate pregnancy and the majority of such patients will deliver vaginally without difficulty. Occasionally, a deep midline episiotomy is necessary to facilitate the descent of the head which has been impeded by vaginal scarring. In certain instances when there are severe symptoms, extensive repairs or where multiple operations have been performed, the danger of injury to vaginal tissue should be obviated by cesarean section.

(There is one vaginal operation which invariably calls for therapeutic abortion in the event of a subsequent pregnancy—and as far as I know it is the only procedure in this category—and that is the interposition operation. Some years ago we lost a mother at 28 weeks who had had the operation performed without sterilization and who steadfastly refused intervention before viability despite an intractable urinary infection and much local pain. Other similar fatalities are on record.

It is informative to note in Finn's series that there was a 16 per cent recurrence following labor of the original condition for which the major vaginal operation was done. This is

the figure which we should all like to reduce by abdominal delivery in selected cases but correct selection is difficult. Finn's figure of 3 per cent for repeat vaginal operations after delivery is noteworthy but I have no data upon which to evaluate it. In general, if there has been an extensive anterior and posterior repair with good results, we usually elect to perform cesarean section. Cases have to be individualized, however, especially in regard to the degree of elasticity of the vagina and perineum, amount of scar tissue, etc. After a successfully repaired vesical vaginal fistula we always deliver abdominally.—Ed.)

MANAGEMENT OF LABOR IN COMPLETE EXSTROPHY OF THE BLADDER

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Health Center J., 1: 135-138, 1948

The patient whose case the author reports was a 24-year-old white female with exstrophy of the bladder who had previously had bilateral transplantation of the ureters, with adequate urinary continence. She had had 2 previous pregnancies which had resulted in one premature delivery and one miscarriage. She entered the hospital at term with her third pregnancy. Physical examination showed massive scar tissue over the entire pubic area where the bladder had been excised. The fundus was 4 cm. below the ensiform. Pelvic examination revealed protrusion of the anterior cervix from the vagina. The introitus anteriorly was composed of scar tissue. The perineum was hypertrophied. X-ray examination showed the maternal pelvis to be deformed due to hypoplasia of the pubic bones and a lack of the normal apposition of the pubic bones at the symphysis.

The patient had active labor pains for 6 hours and at the end of that time the cervix was 7 cm. dilated and the entire cervical rim presented at the introitus. The patient remained stationary at that level of dilatation for one hour, and the fetal heart tones became poor, so Dührssen's incisions were made. A median-lateral episiotomy was performed and a living female infant was delivered. Blood loss was not unusual and the postpartum course was uneventful.

A review of the literature since 1900 revealed a total of 29 deliveries in 21 patients with this congenital abnormality. Delivery per vaginam was successful in 24 of the 29 cases. It is believed that delivery by cesarean section is indicated only by the existence of other complications of pregnancy. 2 figures.

THE NEWBORN

RUPTURE OF THE LIVER AND SPLEEN IN THE NEWBORN INFANT

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J. Pediat., 33: 195-201, 1948

The incidence of rupture of the liver and spleen in the newborn infant is relatively high, and in one series of 2000 unselected autopsies of the newborn and stillborn, 24 such cases were described. The author reports on 8 cases in his experience of rupture of one or both of these organs. Previously, a high incidence had been noted in larger than normal infants. It was felt that bending and compression of the body, often in association with childbirth, was the most probable etiologic mechanism.

The present series of 8 cases includes 5 with rupture of the liver, one with rupture of the spleen and 2 in which both organs were injured. These were found among autopsies on 121 infants who were stillborn or died during the first 3 days of life. On reviewing the site of hematoma or laceration in these cases, several distinct types were found. The first type occurred at the ligamentous insertions of these organs. The second type occurred over the anterior surface of the liver, and the third type was nonspecific in location.

Search for possible circumstances which would best explain these findings revealed only one plausible mechanism. Compression of the chest with pushing down of these organs would cause tension at the ligamentous insertions, and if sufficient pressure were exerted on the chest, tears would then occur. Compression of the costal margin might well be responsible for the laceration on the anterior surface of the liver. A minority of the lesions of the liver in the present group of cases were not obviously related to this mechanism and were probably due to direct trauma. Large infants and those with a relatively large liver, as it occurs in erythroblastosis or in maternal diabetes, are more susceptible to injury of the liver or spleen. In order to prevent these lesions, not only direct trauma to the abdomen but also pressure on the thorax should be avoided as much as possible.

(This is a valuable and timely reminder about an accident that is probably much more frequent than is generally realized. I have seen at autopsy several fatalities of this type which on retrospect were plainly due to jack-knifing the baby in the course of resuscitation. —Ed.)

BIRTH PRIMACY AND IDIOPATHIC EPILEPSY

J. M. NIELSEN AND F. O. BUTLER

Bull. Los Angeles Neurol. Soc., 13: 176-178, 1948

Recent studies by neuropathologists and experimental neurologists have indicated that birth trauma and asphyxia may be responsible for convulsions occurring many years later. Degeneration of the cortex following such mishaps may eventually lead to the formation of microgyria which may be the focus from which epileptic seizures emanate. In taking a history from the epileptic patient, it is often impossible to uncover definite evidence of birth trauma or asphyxia. This is especially true of short duration asphyxia, yet it now seems highly probable that 3 minutes of asphyxia may suffice to cause epilepsy in later life. Because of the increased incidence of difficulty with the first child, it probably follows that if the above premises are true, the incidence of epilepsy should be higher in the firstborn.

Nine hundred and ninety-two cases with epilepsy were studied and, after excluding all cases of definite postnatal etiology and those with deficient data, there remained 780 cases for analysis. There were 279 firstborns and 501 of subsequent birth. The incidence of known birth trauma was essentially the same in firstborns and in others. On the other hand, of all the epilepsy in the group, 35.8 per cent occurred in the firstborn children. As there was an average of 4.2 children per family and as the remaining 64.2 per cent of cases of epilepsy must be distributed among the remaining 3.2 siblings, the average per sibling of those subsequently born is 20 per cent. The ratio of 35.8 to 20 gives 1.79 to 1. The chances of a firstborn child having epilepsy are therefore 1.79, or a little short of twice that for a sibling of subsequent birth in this group.

GONORRHEA COMPLICATING PREGNANCY AND ITS RELATION TO
OPHTHALMIA NEONATORUM

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The authors have studied 292 pregnant women infected with the gonococcus. This group included 103 white patients and 189 Negro patients. The youngest was 12 years and the oldest 42 years of age, with 86 per cent falling in the group 12 to 29 years of age.

Abortion occurred in 4 cases in this series, but this was compatible with an uncomplicated series and so it was felt that gonorrhea was not an important factor in the causation of abortion. However, gonorrhea associated with other com-

plications during pregnancy was a potent factor in increasing the incidence of puerperal morbidity. The incidence of morbidity in this series was 32.05 per cent. It therefore behooves every obstetrician to institute prompt therapy in such cases. There were 8 stillbirths in the series; apparently infection with the gonococcus has no relationship, as an etiologic factor, in the production of stillbirths.

The babies born of the 292 treated mothers were free from infection, and not a single child developed ophthalmia neonatorum; yet, during the same period, 16 cases of ophthalmia neonatorum were observed in babies born of infected non-treated mothers. Both groups of babies received identical prophylactic silver solution instillation into the conjunctival sac. The authors therefore conclude that the true prophylaxis for this condition is the adequate treatment of the infected mother.

(Studies of this type assume especial importance today because of the widespread interest in discarding silver nitrate in favor of some form of penicillin prophylaxis. For a year we employed as a preventive intramuscular penicillin both to mother and infant; for 4 months we used intramuscular penicillin to the baby and during the past 8 months are using local instillations of penicillin ointment. Our total series of cases in which penicillin in one form or another was used as a prophylaxis against gonorrheal ophthalmia now exceeds 6000 and we have not observed a single example of gonorrheal ophthalmia. We are inclined tentatively to believe that the penicillin ointment will pan out to be the most satisfactory procedure.—Ed.)

ERYTHROBLASTOSIS FETALIS ASSOCIATED WITH RH-POSITIVE MOTHERS

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J. Pediat., 33: 190-194, 1948

Two cases are described in which a clinical diagnosis of erythroblastosis fetal is was made but in neither of which were anti-Rh agglutinins demonstrable.

The first case was that of a gravida i, para 0 who was type A, Rh₀ positive, Hr positive, MN. The baby showed generalized edema and died 40 minutes after birth. Autopsy showed extrahematopoietic foci in the liver and muscle, edema of the body surfaces and subcutaneous tissues, ascites and bilateral hydrothorax and bilateral atelectasis. The father's blood was type A, Rh₀ positive, Hr positive, M. There were no demonstrable antibodies in the mother's blood and the maternal and paternal bloods were completely compatible.

The second case was that of a 23-year-old primipara who delivered a normal male infant. Twenty-four hours after birth the child became jaundiced and the liver and spleen were palpable. Laboratory studies showed the infant's hemo-

globin to be 52 per cent and a blood smear showed 100 normoblasts per 100 leucocytes. The baby was type A, Rh positive, Hr positive, heterozygous; the father was type A, Rh positive, Hr negative, homozygous; and the mother was type O, Rh positive, Hr positive, heterozygous. Her blood had an anti-A titre of 1:4000. After repeated transfusions of type A, Rh negative blood the infant made a complete recovery.

In the first case the diagnosis of fetal hydrops unassociated with erythroblastosis is supported by the following facts: primiparity of the mother, no history of previous pregnancies or transfusions, Rh positive mother, absence of antibodies in the maternal blood, and identical ABO, Rh and Hr groupings of mother and father with complete compatibility of maternal and paternal blood.

Erythroblastosis associated with ABO incompatibilities has been described in the literature. The surprising feature is not that an ABO incompatibility may lead to erythroblastosis, but that it does not do so more frequently. Several factors seem to act as a protective mechanism to prevent the production of erythroblastosis in these cases. The maternal alpha and beta agglutinins are usually of low titre. The placenta acts as a barrier against these agglutinins since they are large molecules. There is relative lack of sensitivity of the fetal red blood cells to agglutination. Alpha and beta antibodies are absorbed by extracorporeal group-specific antigens before they get into the fetal blood stream.

Average anti-A titres may range as high as 1:300 in mothers having normal children. In cases of erythroblastosis the anti-A or anti-B titre is usually above this range. However, cases have been reported with an anti-A titre of 1:32,000 with no apparent effect on the infant. In ABO incompatibilities the titre is not the important factor; the functions of the protective mechanism apparently are the determining factor in preventing or producing erythroblastosis.

OPERATIVE OBSTETRICS

CESAREAN HYSTERECTOMY AT THE CHICAGO LYING-IN HOSPITAL

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J. A. M. A., 137: 1017-1023, 1948

This report is an analysis of the authors' indications for cesarean hysterectomy and of the complications, and an explanation as to why the removal of the uterus, if properly carried out, will have the lowest mortality in infected patients.

Harris, in 1922, reported on 64 cesarean hysterectomies performed at Johns Hopkins Hospital with a mortality rate of 4.7 per cent, corrected 1.6 per cent, with no deaths from infections, showing what could be done before the days of blood transfusions and antibiotics.

Reis and De Costa recently reviewed the history of cesarean hysterectomy in the United States. They collected 25,028 cesarean sections and only 636 hysterectomies, an incidence for the latter of 2.5 per cent, and a mortality of 5.2 per cent. The incidence and mortality in their own series were 4.5 and 0 per cent, respectively. The morbidity was much less than what they found after cesarean section; this they attributed to the fact that hysterectomy removes the potentially infected thrombotic placental site and to the substitution of a short incision with opportunity for spontaneous drainage for the longer buried uterine incision.

In the present study the writers exclude hysterectomies in cases in which the uterus ruptured before delivery, but they include patients with separations of the old scar found at the time of cesarean section without any escape of uterine content. Since 1931 there have been 153 cesarean hysterectomies performed on patients who were 30 weeks or more pregnant. The writers believe that elective cesarean hysterectomy has less mortality than elective cesarean section, and in patients past 35 years of age they favor hysterectomy to tubal ligation.

The operation is more difficult than removal of the nonpregnant uterus because of the size of the organ and the dilatation in the lower segment and cervix. It requires about the same amount of time for the experienced operator to perform cesarean hysterectomy as for laparotrachelotomy. The blood loss is not increased and is usually reduced. There is a proper time for the performance of cesarean hysterectomy; it should not be used as a last resort. If the indication is potential or actual infection of the uterus, it is necessary that spill be kept at a minimum, but most important is the complete removal of uterine tissue. The transverse incision must be below the level of the internal os if there is no cervical effacement, and at, or within 2 cm. of, the external os if there is a lower uterine segment. The cuff is closed in layers, using interrupted surgical gut sutures if

there is infection, and completely peritonized with the bladder flap. In infected or potentially infected cases peritonitis routine is necessary for 48 to 96 hours or until the patient's condition warrants oral fluids. During this period adequate supportive treatment is necessary and sufficient parenteral fluid must be given to insure a urinary output of at least 1,000 cc.

The indications for hysterectomy were as follows:

Myoma.....	44 plus
Infection.....	19
Potential infection.....	14
Couvellaire uterus	
Multipara.....	6
Hemorrhage.....	6
Placenta previa	
Multipara.....	6
Accreta.....	2
Placenta accreta.....	2
Tubal ligation failed.....	6
Diseased organ (2 or more cesarean scars).....	11
Thin scar	5
To sterilize; 35 plus years	14
To sterilize; toxemia; 35 plus years.....	4
Ventral hernia.....	2
Uterine hemorrhage.....	3
Carcinoma of cervix.....	4
Miscellaneous.....	5

Over two-thirds of the patients were 30 years of age or older, and over two-thirds had 2 or more children.

The morbidity and duration of fever are given in the authors' Table 4. Potentially infected patients are those in labor and/or with ruptured membranes of more than 24 hours' duration. The criteria for an infected patient are as follows: (1) labor and/or ruptured membranes for 48 hours or more associated with: (a) temperature of 100.4 degrees F. or more, (b) chills, (c) positive blood culture, and (d) large numbers of bacteria in the amniotic fluid; (2) repeated unsterile vaginal examinations; (3) foul-smelling amniotic fluid; (4) labor after attempts at delivery; (5) when a bag, bougie or pack has been in the uterus; (6) more than 12 rectal or 6 vaginal examinations.

Six patients had peritonitis, although the characteristic signs and symptoms of peritonitis were lacking. Two patients had paralytic ileus, presumably without peritonitis. One patient had pelvic thrombophlebitis and one a pelvic abscess. Three patients had serious respiratory infections. Pulmonary embolism occurred in one case. Hemorrhage from the cervical stump occurred in 2 patients on the tenth day and was treated by clamping for 48 hours. Infection of the abdominal wound occurred in 3 patients, and infection of the urinary tract in 3 cases. Two patients sustained bladder injury, one requiring subsequent repair. A serious complication was the ligation of both ureters in 2 patients. The abdomen was reopened and the constricting sutures were cut. One patient required a subsequent nephrectomy for uretero-vaginal fistula and in the other case one ureter

was implanted in the bladder wall and the other in the skin, the kidney being removed subsequently.

There were 10 stillbirths and 8 neonatal deaths, a total uncorrected fetal mortality of 11.8 per cent, which is twice that for cesarean section and 4 times that for all types of delivery. Abruptio placentae, placenta previa and prolonged labor are all characterized by a high fetal mortality and comprise one-third of the series.

The one patient who died was a 32-year-old gravida X, para VI with diabetes, chronic rheumatic heart disease and late pregnancy toxemia. At 37 weeks she was admitted with ruptured membranes, and shortly thereafter began having contractions. After 21 hours of labor with strong pains for 6 hours and ruptured

TABLE 4
Morbidity and duration of fever

TYPE OF CASES	NORMAL	38-38.9 c.*	39-39.9 c.†	40 c.+‡	TOTAL
Clean Cases.....	59-49.0%	47-39.0%	10- 8.0%	4-3.0%	120
Potentially Infected.....	6-50.0%	4-33.0%	2-17.0%	0-	12
Infected.....	6-29.0%	10-48.0%	3-14.0%	2-9.0%	21
Total.....	71-46.0%	61-40.0%	15-10.8%	6-4.0%	153
DURATION OF FEVER					
1 day		15 -19.%	7 -9%	3 -3%	
2 days.....		17 -21.%	4 -5%	1 -1%	
3 days.....		19 -23.%	2 -2%		
4+ days.....		10 -12.%	2 -2%	2 -2%	
Average—days.....		4.3-53.5%	3.2-13.7%	2.8-3.9%	

* 100.4 to 102 F.

† 102.2 to 103.8 F.

‡ 104 F. or higher.

membranes for over 23 hours, a cesarean hysterectomy was performed. She died on the tenth postoperative day. It was felt that she at first had localized peritonitis and that had she been given the routine treatment for peritonitis the outcome might have been different. However, because of a difference of opinion this was not carried out.

The authors conclude that cesarean hysterectomy in the treatment of the infected patient—whether the infection is due to cephalopelvic disproportion, obstruction from tumors, fetal malposition, unsterile examinations or faulty mechanism of labor—should have a mortality of less than 2 per cent. If it is an elective operation the mortality should be less than one per cent. 1 figure.

(This paper has 2 objectives as I see it. The first is to show that cesarean hysterectomy is a safe procedure which in good hands should yield a maternal mortality of less than 2 per cent; the second is to maintain that it is the best way of treating infected or potentially infected cases. In regard to the first claim, there can be no great doubt about this. During

the period covered by the above study we have performed 162 cesarean hysterectomies with 2 deaths, or with about the same mortality as that reported by Dieckmann and his associates, and I imagine many other clinics could show figures as good or better.

In regard to the second claim, namely that cesarean hysterectomy is the best way of treating infected or potentially infected cases, I have the old fashioned notion that the best way to treat an infection is to kill the bacteria. Arthur B. Hunt, in his discussion of the above paper, reported the experience of the Mayo Clinic with sulfonamides and antibiotics in conjunction with low cervical cesarean section in potentially infected cases and stated that their results were good. In the interval since this paper was presented (June, 1947) further evidence has been accumulating that the great majority of organisms responsible for puerperal infection are vulnerable both in vitro and in vivo to penicillin. The most recent evidence on the question is the careful study of Douglas and Landesman (Am. J. Obst. & Gynec. 56:422, 1948). In the light of their experience with the early use of penicillin and sulfadiazine they believe that, in the potentially infected cases, the transperitoneal low flap section may be used without any additional risk to the patient; furthermore, that many cases receiving early and continued prophylactic drug therapy with labor over 48 hours may be classified in the potentially infected group. They feel, however, that the mismanaged and neglected cases with repeated attempts at vaginal delivery and no prophylactic drug therapy, will be candidates for extraperitoneal section or cesarean hysterectomy. With this I would agree, at least at the present time. As to the relative merits of the 2 operations in these very dire cases, this question was discussed in an editorial note in the Survey 2: 663, 1947.—Ed.)

SPINAL ANESTHESIA FOR CESAREAN SECTION

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New Orleans M. & S. J., 101: 19-22, 1948

The purpose of this paper is to study in more detail and to elucidate the hazardous features, if any, of spinal anesthetic for cesarean section.

From January, 1945, to September, 1947, 208 cesarean sections were performed under spinal anesthesia. The patients' ages ranged from 16 to 46. Physical and laboratory findings were negative in 89 per cent of the cases. Seven per cent presented specific contraindications to spinal anesthesia (abnormalities in blood pressure, chiefly hypertension). The remainder presented complications which do not contraindicate spinal anesthesia.

No premedication was given in 25 per cent of the cases. The remainder received atropine or scopolamine in combination with a short-acting barbiturate within the hour previous to induction of anesthesia.

The site of injection was the third or fourth lumbar interspace. The anesthetic drug was made hyperbaric by weighting it with 10 per cent glucose. Pontocaine was used in 54 per cent of cases, Nupercaine in 37, PT-19 in 5 and Novocaine in 4. Satisfactory anesthesia was obtained using much smaller doses than those employed for general surgery.

Hypotension was a constant complication; the blood pressure fell in every case. In 69 per cent of cases the systolic pressure dropped below 100 mm. Hg. This fall occurred on the average of 5 minutes after the establishment of anesthesia. The hypotension was combatted by the use of intravenous ephedrine. A very effective technic is a combination of intravenous and intramuscular injection, which was used in 45 cases. In 13 per cent of cases a hypotension appeared after the operation was well under way; this was effectively overcome by blood and fluids.

Immediately after delivery of the infant, the blood pressure rose, somewhat abruptly, to above pre-anesthetic levels in 78 per cent of cases. The pulse rate slowed after delivery in 72 per cent. Restlessness, noted in 5 per cent of cases, was overcome by intravenous morphine after delivery. Nausea and emesis occurred in 7 per cent of cases, mostly under PT-19. No fetal deaths occurred, and the majority of babies cried spontaneously.

Mild postoperative headache occurred in 2 per cent of cases, and headaches (not considered typical post-lumbar-puncture headaches) occurred in 4 per cent. Urinary retention requiring catheterization was present in 5 per cent of cases.

Obviously, the chief hazard in spinal anesthesia for cesarean section is the sudden, precipitous, severe hypotension encountered. It is the authors' belief that the elevation in blood pressure occurring immediately after delivery of the fetus is due to the release of abdominal pressure with subsequent improvement of the venous return to the heart, causing an increase in cardiac output.

Fatalities from spinal anesthesia are the result of either circulatory or respiratory failure. If respiratory failure is recognized and immediately treated with artificial respiration, the outcome is favorable if the respiratory failure is due to paralysis of the intercostal muscles and diaphragm. Circulatory failure leads to a decrease in blood flow through the cerebrum which is followed by respiratory failure. Herein lies the hazard of spinal anesthesia in cesarean section. For some time it has been known that patients with increased intra-abdominal pressure develop a serious degree of circulatory failure when spinal anesthesia is induced. Pregnant patients respond in this manner. Immediate institution of therapy to combat this circulatory collapse is necessary. For this reason, it is unwise for the obstetrician to assume the dual role of operator and anesthetist, and if he is compelled to act as both he had best avoid spinal anesthesia for cesarean section.

(Doctors Roman and Adriani have presented a series of 208 cesarean sections performed under single injection spinal anesthesia. In this report they have emphasized certain hazards associated with this technic. The complication of hypotension which occurred in 69 per cent of their cases is one of grave significance to the mother, and of even more potential hazard to the baby in utero.

If a blood pressure of less than 80 millimeters of mercury systolic is maintained over several minutes in the presence of strong uterine contractions, the result to the baby is that of disastrous anoxia. In such situations it is conceivable that the contracting tone of the uterus is greater than the hypotensive systolic pressure.

Therefore, if the baby and mother are to be protected from this complication, all avail-

able safeguards should be readily at hand and in minute by minute use in those cases undergoing this type of surgery. These safeguards are: (1) intravenous fluids administered through an indwelling large gauge intravenous needle to compensate the bloodless phlebotomy of the lower extremities and viscera resulting from spinal anesthesia; (2) prophylactic vasopressor drugs administered in regulated doses before, during or after the spinal anesthetic, to maintain normal blood pressure in the hypotensive and normotensive group, and to permit safe moderate reduction in the hypertensive group; (3) 100 per cent oxygen inhalation to enrich the hemoglobin and plasma saturation and thereby increase the availability of oxygen for the baby and for the maternal tissues; (4) the safeguard of autotransfusion by elevation of the maternal lower extremities at right angles with the long body axis is an important technic which should be appreciated by all who use this type of anesthesia; (5) the additional safeguards associated with the continuous types of spinal anesthesia permit administration of safer, smaller preliminary and maintenance doses. Furthermore, with such technics, as with no other in anesthesiology, excessive amounts can be withdrawn in hypertensive patients. Clifford Lull has recently reported more than 1000 consecutive cesarean sections with continuous spinal anesthesia without anesthetic mortality. To this number I can add an additional 700 in 3 clinics without maternal mortality.

There is no question that the baby in a properly executed continuous spinal anesthesia for cesarean section is spared pharmacologic transplacental intoxication. A human mother at term weighs 55 billion milligrams. With only a minute fraction of the quantity recommended in most textbooks, complete anesthesia can be obtained with less than 30 mg. of metycaine or procaine or the equivalent in the average case.

The problem of headache following entry into the subarachnoid space is worthy of a treatise of its own. The recent work of Ahearn (New York Medical Journal, August, 1948) presents a possible solution for obstinate cases with the careful aseptic replacement of lost spinal fluid with saline. We have substantiated his results on four occasions.

The danger of respiratory impairment and failure with single dose spinal anesthesia can be diminished with the hyperbaric technics. They can be abolished with the continuous technics which utilize the principle of the test dose and a slower segmental development of somatic anesthesia.—Robert A. Hingson)

Maternal Mortality Reports

(Secretaries of Maternal Mortality Committees are invited to submit selected cases of maternal deaths, with analyses appended, for publication in this section of the Survey. Cases should be chosen on the basis of educational value, not because of rarity. For obvious reasons complete anonymity will be maintained.

Readers should note that the comment which follows each case history represents the opinion of the Committee concerned and does not necessarily reflect the attitude of the Editors.)

CASE NO. 68

The patient was a registered, white private 22 year old primigravida with negative serology, unknown Rh factor and incompletely measured pelvis whose last menstrual period is said to have begun on August 5, 1946, to make her estimated date of confinement May 12, 1947, but there is ample reason to assume that the menstrual history is incorrect and that the estimated date of confinement should be later than calculated.

The past health is said to have been good and complicated only by an appendectomy 2 years before and by vomiting 6 months before conception, believed to have been due to adhesions and relieved by barbiturates. Nothing specific is known of the family history.

The first prenatal visit occurred on October 22, 1946 (presumed 11 weeks gestation). The Kline test was negative, no blood count was made and the Rh was not determined. Only the external inlet pelvic measurements are recorded. The obstetrical conjugate is given as 11.0 cm. but in the absence of a diagonal conjugate one wonders from what this calculation was made. No preadmission blood counts were obtained. Prenatal visits were of adequate frequency. In the 25th week of gestation the patient's husband appeared with specific urethritis and even though the patient's vaginal smear was negative for gram-negative intracellular diplococci, she was given 2 large doses of penicillin prophylactically. On April 14, 1947, (36 weeks gestation according to menstrual history and 2 weeks after the previous visit) she complained of mild headaches and presented marked edema of the legs, vulva and abdominal wall, all of unknown duration. She had gained 10 pounds in the previous 2 weeks and a total of 37 pounds, now weighing 197 pounds. Blood pressure was 175/110 with 4+ proteinuria. Hospitalization for treatment of the severe preeclampsia was recommended but she was allowed to go home and was not actually admitted until some 8 hours later.

She was admitted to the hospital one evening but not even the ordinary admission observations of temperature, pulse and respiratory rates made until the next morning. At that time bradycardia was recorded and blood pressure 170/130 with 4+ proteinuria. It is assumed that therapy was then begun. It was along usual conservative lines but without sedation. This was continued for days. On the third hospital day penicillin was begun because of pus in the urine. By the fourth hospital day her veins had been so badly damaged that intravenous therapy was intermittent. After 7 days of conservative therapy without apparent improvement in her toxemia state, her physician finally awakened to the fact that he was not going to be able to carry her to term nor to decrease the severity of her toxemia. At this time the general practitioner called a specialist by telephone and presented the known facts. The latter recommended elective cesarean section because of the continued severity of the disease and that operation was planned for the following day. It is not possible to understand the policy of continued delay.

While awaiting the next day for operation the patient experienced some sort of spontaneous accident at midnight. The exact nature of this "crisis" is unknown for there was apparently no examination of the heart and lungs and no blood pressure obtained. The

physician is very vague, as he should be in the absence of adequate examination, as regards the specifications of this event, but believes that pulmonary edema was the most likely cause of the turn in events for her respirations are said to have been labored and noisy. In spite of her poor condition the physician decided to proceed immediately with operative delivery. Her pulse rate was 120/m, respiratory rate 24, and blood pressure 190/120. An elective classical cesarean section was performed under local (procain) infiltration anesthesia. Delivery, as is to be expected, did not improve the condition of the patient, and she succumbed 40 minutes after completion of the cesarean section in spite of heroic efforts to the contrary—caffein, nasal oxygen and plasma. The premature child was born alive, was never weighed, is estimated to have weighed approximately 4 pounds but lived only 3 days. It was not autopsied but death is said to have been due to atelectasis. No autopsy was performed on the mother, was not requested in spite of the fact that her "crisis" and immediate cause of death were never clearly understood. Pulmonary edema, from the available information, would appear to be the most likely immediate cause of death. Cardiac failure is unlikely because of the continued hypertension preoperatively and she is said to have had no eclamptic convulsion though may have had eclampsia without convulsions.

Cause of Death. Shock due to cesarean section on a patient in extremis from pulmonary edema due to severe preeclampsia at 33 weeks' gestation.

Preventability of Death. Preventable.

Responsibility for Death. Physician.

COMMENT

Though the prenatal care is known to have been incomplete in certain phases, these were probably noncontributory factors. The excess weight gain should have suggested the possibility of impending toxemia to the physician (27 pounds during the first 33 weeks of gestation), but he instituted no therapy for it. The next error was to delay hospitalization of a patient with severe fulminating preeclampsia though the patient weathered this error also. The therapy for the toxemia should have included some form of regularly administered sedation. However, the most serious error in handling this patient's last illness is the unwarranted delay in effecting delivery. Certainly it did not require a week to prove that conservative therapy was not effective and 2 or 3 days of such should have been ample. Any consultation without actually seeing and examining the patient can hardly be considered adequate. Once the decision to deliver the patient had been made it should not have been postponed until the following day especially in view of the already excessive period of postponement. Certainly, the most serious immediate cause of death was the operative procedure upon the patient who was then apparently already in extremis. There was nothing to be gained in doing this except possibly to salvage the fetus, but even this failed. No autopsy was requested even with all the uncertainty relative to the causes of death. The premature fetus was neither weighed nor autopsied after death. Why it was so ignored is not understood. This death should have been prevented by earlier interruption of pregnancy when no improvement was obtained.

CASE NO. 69

The patient was a 28 year old unregistered private Mexican multipara with unknown blood Wassermann, undetermined Rh factor and unmeasured pelvis, who is said to have been 2½ months pregnant when first seen.

The hospital record contains no information about her past obstetrical career but there is some rumor that she had had 3 previous term or near term pregnancies, and had been advised against subsequent ones. Almost certainly this advice was in the form of mild warning and she was given no contraception. There is no hospital information relative to her past medical or surgical history nor family or menstrual history. She is said to have been in only fair health previously but there is no elaboration upon this statement.

Approximately 2 weeks before death she is said to have had vaginal bleeding but apparently did not consult a physician (2 months' gestation). However, 2 weeks later bleeding was profuse with the passage of clots. She was seen at home by a family physician and hospitalization was recommended. She did not appear at the hospital until some hours later because that time was required to raise enough money for admission as a private patient. When seen in the hospital she was in shock with blood pressure 90/60 and weak pulse 100/m., and appeared anemic and malnourished with shallow respirations but respiratory rate not recorded. She is said to have had moderate generalized abdominal tenderness. Pelvic examination revealed the fetus, approximately 2 months in size, one-half expelled through the cervical os. No routine blood studies were obtained. The attending physician claims to have planned immediate evacuation of the uterus but was advised against such course. The true facts cannot be ascertained for the consultant gave his advice per telephone and never saw the patient. Whether the case was accurately presented in telephone conversation is immaterial. This case is a shining example of the worthlessness of any consultation short of actually seeing and examining the patient.

Stilbestrol (50 mg.) was given orally with 2 tablets of ergotrate while an ampule of pitocin was given intramuscularly with morphine also apparently given at this time or shortly thereafter. There would seem to be no logic for giving such an array of conflicting drugs to a patient with an obviously inevitable abortion. Blood matching without Rh determination was ordered and a transfusion begun 3 hours after admission. The reason for such delay in a hospital with a blood bank cannot be understood. The patient experienced a chill after 400 cc. of the blood had been given. Even this occurrence did not suggest to the attending physician the possibility of Rh incompatibility but the remaining 100 cc. of blood was not given. The patient's blood pressure was now 82/40 with pulse weak and rapid and bleeding only slight. The patient's physician was notified, did not return to the hospital, and an infusion of 500 cc. of 10 per cent glucose in saline was started. Later demerol and hyoscin were given. The patient expired 8 hours after hospitalization without the private physician in attendance and the exact nature of the death is not described. Permission for autopsy is said to have been requested but refused.

Cause of Death. Shock due to transfusion reaction (probably Rh incompatibility) following hemorrhage due to inevitable early abortion.

Preventability of Death. Preventable.

Responsibility for Death. Physicians (original and consultant)

COMMENT

There are herein errors of omission as well as commission. For example, if there was a real emergency, it seems unfair to have delayed hospitalization while money was being raised to make this a private case. Surely the care could have been no worse on a charity service and might have been better. However, upon eventual admission she was in obvious shock from blood loss. The logical course would have been to sedate her, avoid attempting to postpone the inevitable abortion through the use of a large dose of stilbestrol, to immediately obtain a compatible donor in respect to both A and Rh factors, and to empty the uterus without further delay, blood pressure permitting. The logic of the course taken

is not clear. The record is so incomplete that one cannot determine whether excessive blood loss occurred at any time after hospitalization. The only notation is to the effect that bleeding was slight. Moreover, patients with abortions, like placenta previa, rarely if ever succumb to blood loss unless tampered with. These facts lead one to presume that death was due to shock from the transfusion of incompatible Rh blood and not from acute blood loss.

CASE NO. 70

The patient was a registered colored charity 34 year old para 0-0-2-0 with negative serology though a latent luetic, normal pelvis and Rh positive, whose menstrual history is incorrect but who is presumed to have been at term upon delivery on July 11, 1947.

She had a 5-months spontaneous abortion in 1931 with attendance at home by a midwife. In 1940 a similar occurrence with a 6 months abortion is said to have occurred. She had no prenatal care with either pregnancy. The only statement about her past history is that she had "shots" for syphilis in 1942. In spite of subsequent events her past general health is said to have been good. Nothing is known of her family history.

She presented herself for prenatal care at a charity clinic on April 18, 1947, when the pregnancy is presumed to have advanced into the 33rd week. She claims to have had nocturia, dyspnea and ankle edema for the previous 2 months. Both heart and lungs are described as "negative." She had 1+ ankle edema. Pelvic measurements were normal. The fundus uteri measured 25 cm. but with no further specification the measurement is meaningless. It is assumed that it represented the caliper measurement, for McDonald measurement of that magnitude would represent only a 28 weeks gestation. Serological tests were negative and it is assumed she had no further antiluetic therapy. There was no anemia, her blood was Rh-positive and she was apparently considered a healthy colored woman.

Routine or follow-up prenatal visits were well spaced and apparently included minimum requirements. One week later her blood pressure was 130/90 and on May 9, 1947 (35½ weeks gestation) it was up to 145/90 with 3+ edema and with no proteinuria. She is said to have been placed on a "preeclamptic" diet but the meaning of this designation is not described. There was some little decrease in toxemia signs but 2 weeks later she presented a gain in weight of 6½ pounds in the previous week. It is said that she was "put back on" the preeclamptic diet and bed rest was advised as well as a return visit in 1 week. A note indicated that she would be hospitalized if there was no improvement in the toxemia. She returned 18 days later to the emergency room and it is quite obvious that her absence had not been noted and no attempt made to ascertain why she did not return on schedule.

She was admitted in questionable labor with temperature 100, pulse 102/m., blood pressure 185/115, 4+ rather generalized edema, and a trace of proteinuria. The lungs are described as clear but respirations short and moderately fast (rate not given). She had a slight cough. No cardiac murmurs were heard and there was doubtful left-sided enlargement. She was placed on the following regime: 50 cc. 50 per cent glucose with 2 cc. 50 per cent magnesium sulfate intravenously every 4 hours, 500 cc. 20 per cent glucose in water twice daily, salt-poor diet and phenobarbital every 3 hours. She was apparently not yet in active labor. On the following day blood studies were obtained and showed no anemia, no retention of protein metabolites, but reduction in serum proteins. Urine contained a heavy trace of proteinuria. There must have been some labor since admission for the fetal head had descended to station plus 1 and cervix attained 3 cm. dilatation. Rales were heard in both lung bases, the patient was now thought to be a cardiac of Class III variety, and complete cardiac work-up was ordered. There must have been a long prodromal labor or one characterized by uterine inertia for she is said to have had only a 9 hour labor yet delivered on the third hospital day. Sedation consisted of only 100 mg. demerol in addition to the phenobarbital. Delivery was effected by low forceps extraction after episiotomy

under local infiltration anesthesia, 1 per cent novocain in unstated amount being used with undesignated results. The fetus weighed 8 pounds 8 ounces, was stillborn but presumed non-macerated, and there is no indication of when fetal death occurred though it must have taken place in the hospital for the admission examination stated fetal heart tones were 136/m. Pre-delivery blood pressure was 134/80 and estimated blood loss 200 cc. with immediate postpartum blood pressure 120/80. The resident, who delivered the patient, thought her early puerperal condition satisfactory, while the nurses described it as poor. The medical consultant who saw the patient at about this time found her to be in apparently fair condition. However, according to the nurses' notes, blood pressure began to fall after delivery, reaching a low of 80/60 about 3 hours after delivery, after which it climbed again to normal levels. The medical consultant found a systolic murmur over the manubrium and the pulmonic area, heard the most rales in the lung bases, made a diagnosis of "pre-eclamptic uremia with cardiac decompensation," and advised continuation of both digitalis and nasal oxygen which were begun in unstated amounts about 3 hours prior to delivery.

About an hour after delivery she had a chill with fever to 104, pulse rate to 130/m., and respirations 40/m., and for which she was given a sedative, more hypertonic glucose, and started on large doses of penicillin. Though it is not stated, this must have been a puerperal infection. X-ray of the chest taken this day revealed cardiac enlargement and pulmonary congestion indicative of congestive heart failure. It should be emphasized that in labor her blood pressure ranged between 196/130 and 144/102.

On the day after delivery she looked and felt better with blood pressure 130/90, temperature 99, pulse rate 110/m., and respirations 28/m. All veins previously used were now thrombosed but she was taking fluids by mouth and intravenous therapy was stopped. She was apparently weathering the cardiac failure satisfactorily and appeared even more improved on the second puerperal day, but man was not satisfied and started an infusion of pooled plasma which again produced fatal trouble. Only two-thirds of the 300 cc. had been given when she developed a severe reaction with chill and the remaining 100 cc. was not given. Two hours after this reaction she is said to have suddenly developed pulmonary edema and within another 30 minutes her blood pressure was unattainable. She lingered on for more than another hour under heroic treatment and stimulants. Blood chemistry on this day showed considerable retention of protein metabolites with NPN 63 and uric acid 7.8 mg. per cent. Permission for postmortem examination is said to have been requested but not obtained on account of the husband's strong opposition. The fetus was not autopsied and hence there is no way of knowing whether it was luetic or not.

Cause of Death. Cardiac failure due to shock from intravenous plasma given decompensated puerperal woman with severe preeclampsia.

Preventability of Death. Preventable.

Responsibility for Death. Physician.

COMMENT

This seems to have been an unnecessary death. In the first place, the medical profession was too long blind to the real cardiac status, actually failed to make the diagnosis of severe heart disease until decompensation appeared when a layman could have made the diagnosis. This error probably accounted for the delay in hospitalization for evaluation of cardiac status. The earliest signs of toxemia were ignored and too much time allowed to elapse between visits. The clinic physician cannot lay sole responsibility upon the patient for seeing that she returned as requested. Some division of the hospital, in all probability social service, should have visited, called or written this woman to put in her appearance when she failed to keep her appointment. After hospitalization, the

battle was apparently not lost, care in labor, delivery and the immediate puerperium being adequate to allow her to show evidence of returning compensation. The blow which struck the weak spot at the most inopportune time was the pooled plasma. This is not the first maternal death in this fiscal year which was either directly responsible for or implicated in the death. When will this hospital wake up to the real dangers of their pooled plasma? How long will it be before we are faced with the need to again criticize for its use? This discussion cannot be closed without pointing to the fact that this seronegative luetic received no therapy during pregnancy. We don't know whether her offspring was luetic because it did not survive. Neither was it autopsied. However, it succumbed in utero in labor and this suggests the definite possibility of congenital syphilis. Child's death certificate records "Body given to hospital for Medical Research." Its disposal is unknown in that hospital's Pathology Department but there is no record of an autopsy.

CASE NO. 71

The patient was a registered 37 year old Mexican primigravida with normal pelvis, negative serology, positive Rh, whose last menstrual period began on September 6, 1946, making her estimated date of confinement June 13, 1947.

She first appeared for prenatal care on November 5, 1946, in the 9th week of gestation. Her past health had been good without operations or serious illnesses. Her family history was probably noncontributory. Menstrual history was normal. She is said to have been obese, weighing 187 pounds, being 5'3½" tall, and it is assumed that this was her early pregnancy weight. Physical examination revealed no pathology save for the obesity. Pelvic mensuration was complete and revealed a normal pelvis, C.D. 12.5+ cm. and T.I. 9.5 cm. There was a mild anemia with hemoglobin of 70 per cent and 4.32 million red blood cells.

Routine prenatal visits occurred every 2 weeks throughout the period of observation and were complete in every respect. Moniliasis appeared in the 19th week and glycosuria with hydramnios in the 37th week of gestation. The appearance of glycosuria raises the question of whether this patient had clinical or subclinical diabetes and subsequent events also raise this question, but there is no evidence that she was studied for this possibility. In the 2 weeks prior to the discovery of hydramnios she had gained 10 pounds in weight and now presented marked edema of the lower extremities, blood pressure 140/90, but no albuminuria and presumably no other toxemia signs or symptoms. Consultation was had by another competent specialist and the patient was admitted the next day to the hospital for study, rest and x-rays.

X-ray of the lower abdomen showed poor visualization of certain parts of the fetus (obviously due to the hydramnios), yet the roentgenologist refused to make a frank diagnosis of hydramnios and hedged by saying that the findings "were consistent with hydramnios." On the other hand he stuck his neck out too far by saying that the fetus was of term-size without any evident bony deformity when subsequent events conclusively show that the fetus at this stage was already well above average in size. This error on his part is almost certainly largely responsible for certain phases of later treatment. Under therapy with hypertonic glucose solutions, the edema rapidly decreased, the blood pressure rapidly fell to normal, and she was sent home. The record does not indicate the exact period of this hospitalization but was apparently for only a few days. Neither does the record show that any routine blood or urine studies were obtained.

The original physician followed the patient through his office for several days before leaving the city. The consultant took over on June 6, 1947, when the pregnancy was 1 week from term and roughly 2 weeks after discharge from the hospital. She had gained 12 more pounds since the original consultation visit and was now quite uncomfortable with dyspnea

and the fundus uteri 43 cm. above the symphysis pubis (McDonald measurement) when 32 cm. is the average measurement at this stage of pregnancy. The presenting fetal head was not engaged and rectal examination showed the cervix long and thick. She was readmitted to the hospital on this day.

Routine blood studies on this admission showed the same mild anemia as when first seen prenatally and there was no retention of protein metabolites. Therapy consisted of low salt diet, saline catharsis, hypertonic glucose administered intravenously, and mild sedation. Dyspnea persisted. On the 4th day of this admission and one-half week before the estimated date of confinement, on the advice of a competent consultant, membranes were ruptured artificially for induction of labor. The cervix was found 2 cm. dilated and uneffaced with the fetal head unengaged but this was considered more desirable therapy than induction by cesarean section because of the possibility of fetal anomaly associated with the marked hydramnios. One cannot criticize this line of reasoning but the attendants were laboring under false advice given by the roentgenologist and had no idea of the extent of the excessive-size of the fetus, having to depend upon the x-ray consultant since the hydramnios prevented adequate abdominal palpation of the fetus and therefore clinical evaluation of its size. An estimated 1 gallon of amniotic fluid was released and it came away slowly.

Most of the remainder of the story is typical of primary uterine inertia. Labor began 2 hours after its induction and the first stage was never completed though allowed to progress for almost 80 hours. The passage of meconium appeared after 40 hours of labor and fetal heart tones were no longer heard thereafter. The cervix was 5 to 6 cm. dilated at this time and the fetal head at station plus 1. At 63 hours and after some 12 hours without evidence of progress in labor, small doses of intramuscular pitocin were started but only 3 utilized in the next 12 hours of labor. This produced increase in cervical dilatation to 8 cm. and then the decision to end the labor was apparently made without further consultation. Chemotherapy in the form of sulfadiazine had been started after 24 hours of labor because of fever, the maximum in labor being 101.6. The maximum pulse rate in labor is stated to have been 106/m. There is no mention of supportive therapy in labor except for glucose (unstated amount and diluent) given when sulfadiazine was started and one wonders whether more was not indicated.

Under cyclopropane-ether anesthesia given by a nurse-anesthetist, she was delivered with difficulty. Dührssen's incisions were made at 10 and 2 o'clock. Manual rotation from an original LOP to LOA was effected before great difficulty with axis-traction was encountered in delivering the fetal head. Great difficulty was then met with delivery of the shoulders and it was finally accomplished with the assistance of suprafundic pressure by 2 assistants. It had been possible to fracture a clavicle and apparently no attempt had been made to cut it. The abdomen followed with difficulty presumed to have been due to the enlarged and cystic abdomen. Fifty minutes were required to effect delivery. The fetus was stillborn and macerated, weighing 12 pounds 14½ ounces. No other measurements were obtained. Though it is not so stated, it is assumed that this body was not autopsied and the diagnosis of congenital cystic kidneys was made from gross appearance.

During the process of getting the shoulders delivered, the assistants applying suprafundic pressure noted a sensation of something giving. This gave rise to the suspicion of rupture of the uterus. It should be here noted with condemnation that up to this point in delivery the blood pressure had not been taken. It was now 90/50 and glucose and plasma were begun, bringing the blood pressure within 15 minutes up to 104/48. Immediately after delivery of the fetus pituitrin was given, the uterine cavity explored for the possibility of rupture but none was found, the placenta was manually removed, the uterine cavity tightly packed with gauze apparently in anticipation of and not following hemorrhage, and ergotrate was given intramuscularly.

The episiotomy which had not extended was repaired as were the cervical incisions, but there is no statement of whether they had extended during delivery. An upper vaginal laceration was likewise repaired. The whole operative procedure required anesthetic for

2 hours and 10 minutes. The patient lived only 10 minutes after the end of the operative procedure and anesthetic, death said to have been due to shock. She was receiving intravenous glucose and plasma at the time of death and was believed to have been in fair condition with systolic blood pressure 104 and pulse rate 120/m. at the end of the operation. Matching of blood was not ordered until an hour prior to death. The estimated blood loss was only 200 cc. Immediately after death the uterus was found to be well contracted. Permission for postmortem examination was requested but refused.

Cause of death. Shock following traumatizing delivery of a large excessive-sized stillborn and macerated fetus from a term pregnancy associated with mild anemia, hydramnios, and a fetus with presumed cystic kidneys after prolonged labor induced by membrane rupture and characterized by primary uterine inertia and intrapartum fever.

Preventability of Death. Preventable.

Responsibility for Death. Physician.

COMMENT

This case does not easily lend itself to much obvious adverse criticism. Prenatal care was certainly of the highest order and more could not have been done. The study would be more complete, however, if it were known whether this patient had been a subclinical diabetic. The induction of labor via membrane rupture can not be criticized. It was certainly the method of choice under the circumstances and with the available false impressions about fetal size. The first wrong step to arrive at this maternal death was the apparent explicit acceptance of the roentgenologist's diagnosis of fairly normal fetus. The physician who cared for this labor once used the McDonald measurement (i.e., before membranes were ruptured). Why he did not repeat this mensuration after much or most of the amniotic fluid had drained away is not understood. To have done this simple test would have proven to his satisfaction the great error of the roentgenologist's interpretation of fetal size. It is freely granted that clinical impressions of fetal size below $5\frac{1}{2}$ pounds and above 9 pounds are apt to be far from precise. On the other hand, one cannot refrain from arguing that careful abdominal palpation after liberation of the excess amount of amniotic fluid should have given the unmistakable impression that this fetus was huge. It would seem that we should no longer accept the roentgen impression of fetal or of maternal pelvic size if these do not confirm clinical impression. It has been shown time and again that the roentgenologist's knowledge of obstetrics is woefully inadequate. In this particular case, the macerated fetus weighed essentially twice as much as the average living fetus at term. He can not argue that one-half the weight or development of this fetus occurred between the day of the x-ray of this case and the date of fetal death in utero, a period of 3 weeks. If the clinician in this case had suspected excess size of the fetus, he could have proven it to his satisfaction and to that of the roentgenologist by re-x-ray after membrane rupture. Had the great size of this fetus been suspected a more safe delivery for the mother would obviously have been selected. There could have been no accusation made had cesarean section been done for delivery of

this fetus with abnormalities inconsistent with life, even after its death in utero. However, since vaginal delivery was desired it was hardly wise to proceed with what could have been at best anticipated as difficult when the forceps delivery was hardly more than midpelvic in type, in an elderly primigravida with probably more than average rigid musculature, with 8 cm. cervical dilatation, and in a patient who was a poor surgical risk due to her general configuration and long labor. To say that no further progress would occur is simply stating clinical impression which can never be proven or disproven. There is every reason to believe that ultimately and infinitely more safe circumstances for delivery would have presented themselves. If they had not, then craniotomy and morcellation would have been less shocking to the patient. That there was not uterine rupture had been only partially proven. If our record of this labor is complete, there is reason to assume that this patient received inadequate supportive therapy in labor. Certainly it was inadequate for labor since she received no intravenous glucose preliminary to delivery. That request for blood matching was delayed too long is quite obvious since the order for it came fully 15 minutes after completion of the delivery of the fetus. I believe the handling of this labor affords more proof that too much reliance is placed in glucose to the exclusion of whole blood or of plasma for the treatment of shock and/or hemorrhage. One wonders, too, about the necessity for adding the trauma of manual removal of the placenta to this already badly battered patient. I wonder whether the consultant would have approved of the course taken if he had known and examined the patient prior to delivery. It is regrettable that an autopsy was not performed on this child in order to ascertain the nature of abdominal distension. It appears that permission for postmortem examination on the mother was urgently requested but refused and would have been most helpful in determining further the absence or presence of uterine rupture.

Gynecology

ENDOCRINOLOGY

EFFECTS OF VARIOUS ESTROGENIC PREPARATIONS ON THE VAGINAL MUCOSA

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Am. J. Obst. & Gynec., 56: 269-280, 1948

Many preparations having ovarian follicular hormone activity are now commercially available. The question discussed in this report is: on what basis shall we choose our estrogen? A total of 71 studies in 55 postmenopausal women was made to determine the relative effects of 7 different estrogenic preparations. The drugs studied were estradiol in sesame oil, estradiol in propylene glycol, estradiol dipropionate in sesame oil, estradiol benzoate in peanut oil, estradiol benzoate in propylene glycol, estradiol and estradiol benzoate in sesame oil, and estradiol and estradiol benzoate in propylene glycol. Vaginal smears were obtained prior to injection and at 12-hour intervals following administration of a single dose. Periods of observation ranged from 60 to 377 hours.

Three subjects gave no evidence of response, while in 24 tests there was an alteration in the type of smear without follicular reaction, and in 44 subjects this response was present in varying degree. The degree of follicular reaction and the amount of hormone injected could be directly correlated. An inverse relation was found to exist between age and the height of the follicular reaction. The range of lag time, or time between injection and response varied from 42 to 180 hours. An inverse relation existed between the lag time and the amount of hormone injected. The age of the subject apparently was not a factor in the lag time. The range of duration of follicular reaction varied from 12 to 200 plus hours. In general, a higher dose tended to produce alterations of longer duration in the vaginal epithelium.

It was concluded that a single one milligram dose of either free estradiol or estradiol esters in sesame oil, peanut oil or propylene glycol is sufficient to stimulate growth and, at least, partial maturation of the vaginal epithelium in most subjects. There was some indication that the esters of estradiol in oily menstrua act more rapidly than either free estradiol or its esters in propylene glycol. Full maturation of the vaginal epithelium of postmenopausal women is dependent, to great extent, on the amount of hormone injected and on the age of the patient. These studies, however, place further emphasis on the fact that the doses of estrogen necessary for relief of climacteric symptoms are not quantitatively related to those required to produce full estrogenic response in the vaginal epithelium. 4 figures.

(It is the last sentence of the above abstract which I believe deserves especial emphasis. The target of estrogen therapy for menopausal symptoms is not the vaginal response, but the vasomotor symptoms which the patient presents, and the two effects do not parallel each other. A good many years ago it was clearly shown that the vasomotor symptoms are often relieved with doses not capable of evoking a full vaginal response. All of the 40 or 50 available commercial preparations are estrogenically potent, although there are wide variations in potency and duration. However, all of them are effective in the relief of menopausal symptoms when these are severe enough to need treatment, if one employs the proper dosage, which is based upon their individual degree of potency. For most indications the oral estrogens, of which there are a good many available, are always to be preferred to those intended for hypodermic administration.—Ed.)

THE ROLE OF SEX HORMONES IN THE DIFFERENTIATION OF THE SEXES AND IN SEXUAL ABNORMALITY

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Proc. Inst. Med. Chicago, 17: 66-68, 1948

The individual inherits his sexual predisposition, depending on the presence of male or female determiners in his genes or, more correctly, on a preponderance of one or the other determiners. Admitting the presence of the embryonic rudiments of both reproductive systems in every normal individual, it is now quite general to account for sexual differentiation on the basis of hormones secreted by the embryonic sex glands. The embryonic hormones are believed to stimulate homologous sex character development by acting upon the reproductive system and the potential secondary sex characteristics, and to inhibit or drive out of existence the heterologous characters potentially present. Therefore, the intersexual or hermaphroditic condition is blamed upon faulty function of an embryonic sex gland.

The author has attempted to substantiate this theory, using for his experimental purposes chemically pure sex hormones and the developing pouch young of the marsupial opossum. The administration of androgens to the young of both sexes during the time of their reproductive development provided some expected stimulation for the male system. In the female, the ovaries were not injured, and the oviducts, uterus and lateral vaginal canals were precociously stimulated. Estrogens, on the other hand, had no effect upon the testes and stimulated rather than inhibited the male ducts.

The problem was further approached by surgical removal of the gonads from both sexes at a stage when both embryonic sex duct systems were still present. Further sexual differentiation proceeded just as well in the operated young as in the unoperated controls.

Such observations have raised the question whether reproductive duct development is, in fact, under the control of hormones secreted by the developing gonad

or, indeed, whether embryonic sex glands actually secrete hormones during their embryonic development. It seems to be clearly demonstrated that the differentiation of the embryonic sex duct systems does not depend upon the presence of a gonad to secrete hormones which would guide their respective destinies, and it is presumed that the genetic equipment, rather than hormones secreted by embryonic glands, is the operating mechanism.

It is a well-accepted fact that reproductive structures, when formed or when preserved atypically in the organism by any means, respond to sex hormone stimulation. In a similar manner, unusual remnants of the embryonic reproductive system that happen to remain in the organism can frequently respond with remarkable growth when hormones are present. This condition is thus fundamental to the sexually abnormal type of intersexual or hermaphrodite which may show well developed organs of both sexes. It is felt, therefore, that the hermaphrodite results from a faulty genetic mechanism rather than from faulty secretion of sex hormones by an embryonic gonad.

(The author, a distinguished investigator in the endocrine field, bravely tackles a fundamental problem which has been a bone of contention for many years, and his conclusions are similar to those arrived at by certain other investigators, notably the late Josef Halban more than a generation ago. Everyone apparently accepts that the determination of sex is a matter of chromosomes, and everyone believes that the endocrine glands are of importance in the later unfolding of sex characters, but there is little knowledge as to the relation between these two factors.

Moore's work appears to discredit the importance of the embryonic sex glands which have been thought by some to possess a hormone function, although no one, so far as I know, has established this beyond doubt. Even the later function of the sex glands is probably in the nature of an auxiliary force dependent upon the masculine or feminine direction imported by the genetic sex balance of the chromosomes. Moore's interesting experiments appear to bear out this concept.—Ed.)

GONADOTROPHIC HORMONE THERAPY IN MAN COMPLICATED BY ANTIHORMONE FORMATION

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Am. J. Obst. & Gynec., 56: 521-526, 1948

A combination of sheep anterior pituitary extract and human chorionic gonadotrophin (Synapoidin) was used in the treatment of 30 women and 4 men for various reproductive disorders. Correlated studies were made to determine whether this combination of gonadotrophins will excite antihormone formation. It was found that these inhibitory substances did not develop in 30 of the 34 cases, and that generally they will not do so in less than 5 months. In 4 cases of functional bleeding, definite antihormone titers were recorded after 5 months of therapy. The presence of antihormones could be correlated with the clinical

response; that is, the failure of the patient to continue to respond to therapy coincided with the time at which antihormones were detectable. These inhibitory substances disappear in 3 months.

The largest total dosage used in this study was 750 units, given to a patient during 4 months, and failing to elicit anti-hormone formation.

It is most logical to assume that the sheep anterior pituitary extract of this hormone combine is responsible for the antihormone formation. In general, chorionic gonadotrophin in human therapy has not been antihormonic. It is well known that equine gonadotrophin will elicit antihormone formation. The nitrogen content of the preparation does not permit one to draw conclusions at the present time as to the antihormone-forming abilities of any one of two preparations from different sources.

(This study is of interest precisely because it is especially the gonadotrophic hormones which have been incriminated by the work of certain previous investigators as evoking the production of anti-hormones. So far as I know, this change has never been substantiated in the case of estrogens or thyroid, and, as a matter of fact, the whole doctrine of anti-hormones originally enunciated by Collip is still a rather hazy one. The majority of investigators believe, like the present authors, that these supposed antihormonal reactions are not really specific, but that they are evoked by the small amounts of protein present in most of the gonadotrophic preparations, such as the one with which Leatham and his collaborators employed in their study. Incidentally, I may add that I have seen no serious allergic reactions with this particular preparation, which I have often employed in clinical practice, although it is certainly wise to precede its administration with a simple intradermal test.—Ed.)

THE RESPONSE OF THE HUMAN FETAL REPRODUCTIVE SYSTEM TO THE ADMINISTRATION OF DIETHYLSTILBESTROL AND TESTOSTERONE PROPIONATE DURING EARLY PREGNANCY

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Endocrinology 42: 370-378, 1948

With the recent trend toward the use of female sex hormones in early pregnancy it is particularly interesting to observe the effect of this artificial introduction of hormones on the fetal gonads. Most workers agree that there may be some modification in the pattern of these organs. The hormonal action is not specific; both heterologous and homologous organs are stimulated by excessive amounts of hormones. Sex hormones were given to 15 women with normal gestations. The fetuses in 7 of the cases were available for complete histologic studies. Four patients received diethylstilbestrol and 2, testosterone propionate. Six fetuses were male, weighing from 160 to 360 gm. One fetus was female. Ten fetuses removed by hysterectomy were used as a control group.

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Moore's work appears to discredit the importance of the embryonic sex glands which have been thought by some to possess a hormone function, although no one, so far as I know, has established this beyond doubt. Even the later function of the sex glands is probably in the nature of an auxiliary force dependent upon the masculine or feminine direction imported by the genetic sex balance of the chromosomes. Moore's interesting experiments appear to bear out this concept.—Ed.)

GONADOTROPHIC HORMONE THERAPY IN MAN COMPLICATED BY ANTIHORMONE FORMATION

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Am. J. Obst. & Gynec., 56: 521-526, 1948

A combination of sheep anterior pituitary extract and human chorionic gonadotrophin (Synapoidin) was used in the treatment of 30 women and 4 men for various reproductive disorders. Correlated studies were made to determine whether this combination of gonadotrophins will excite antihormone formation. It was found that these inhibitory substances did not develop in 30 of the 34 cases, and that generally they will not do so in less than 5 months. In 4 cases of functional bleeding, definite antihormone titers were recorded after 5 months of therapy. The presence of antihormones could be correlated with the clinical

about the chemical structure of the steroids in the tumor tissue. A study of the steroids in the urine revealed that in the gynecomastia the excretion of 17 Ketosteroids was 4 mg. per day and small amounts of estrogen were demonstrated. The patient with virilization excreted 22 mg. 17 ketosteroids; less than 1% of this was of the beta fractions. Pathological study of the 2 tumors revealed that each had large polyhedral cells of no particular arrangement. No essential difference was detected; each neoplasm resembled the prenatal zone of the adrenal.

The author presents a table classifying diseases of the adrenal cortex according to their hormonal manifestations. He defines the adrenogenital syndrome as a disorder in which there are evidences of excessive androgen production with excessive or deficient cortin and the Cushing syndrome as a disorder with signs of excessive cortin, usually with evidence of androgen increase and sometimes with estrogen increase.

On the basis of his classifications and definitions 70 cases of adrenal tumors in children under 12 years were studied and tabulated. Ten cases of feminizing adrenal tumors in adult males were also analyzed. It was noted that the patient presented here was the only case of a feminizing adrenal tumor in a child yet reported. 7 figures. 3 tables.

(While this paper is only partly of gynecological pertinence, it will be of the greatest interest and value to everyone interested in that still hazy field of endocrinology dealing with the relationships between the adrenal cortex and the gonads. To my mind this great undiscovered endocrine country is one of rich potentialities, and some day the gold rush will begin. The perplexing nature of corticogonadal relationships is shown by the fact that in the 2 children of about the same age reported by Wilkins the adrenal cortical tumors presented identical histological pictures, but produced masculinization changes in the female child and feminization in the male. Wilkins also renders a service in reviewing the literature of the subject so completely, and in pointing out that in the 53 girls reported to have had cortical adenomas in only 31 did the syndrome fulfill the definition of the simple adrenocortical syndrome, in which no evidence of cortin disturbance or deficiency is combined with the masculinization phenomena. The remaining 22 had symptoms suggestive of the Cushing syndrome, with obesity or other evidences of hypercorticism.

To the gynecologist familiar with the heterosexual phenomena which are produced by cortical tumors in women, and the heterosexual type of precocious puberty seen when such tumors occur in female children, it will be of interest to note that in 11 reported cases gynecomastia has been noted from similar tumors in males, Wilkins' case being the only one in which such a feminizing tumor has been found before puberty. Finally, Wilkins' paper is of value in its report of the hormone studies in his own 2 cases and in his review of similar studies in the small proportion of reported cases in which these have been carried out.—Ed.)

In no instance was it possible to distinguish between a fetus of a mother who had received diethylstilbestrol or testosterone propionate from 1 of the control group. The authors conclude that these drugs administered in therapeutic doses in early pregnancy will not adversely affect the development of the genitals in the male fetus.

(As the authors state, there is an increasing resort to hormone therapy in early pregnancy, especially in the management of threatened or habitual abortion. Progesterone has been thus widely employed, although the initial enthusiasm for this plan has waned a good deal in the past few years. More recently estrogens alone or estrogens with progesterone have gained some popularity, although it is too early as yet to say whether they will become lasting additions to the therapeutic armamentarium. Certainly no one appears to have felt that they were harmful to the fetus, but it is reassuring to have direct evidence on the basis of histological study. Regarding testosterone, which so far as I know has no rational indication in early pregnancy, one might perhaps feel a subconscious apprehension, but Potter's studies indicate that this likewise, at least in the doses employed, apparently has no adverse effect upon the development of the genitalia of male fetuses.—Ed.)

A FEMINIZING ADRENAL TUMOR CAUSING GYNÉCOMASTIA IN A BOY OF FIVE YEARS CONTRASTED WITH A VIRILIZING TUMOR IN A FIVE YEAR OLD GIRL

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J. Clin. Endocrinol. 8: 111-132, 1948

A 5-year old boy was brought into the clinic because of large, well-developed breasts. General health and growth were normal. X-ray revealed a calcified mass visible above the right kidney.

It was believed that the boy had a tumor producing an estrogenic substance and an abdominal exploration was undertaken. Exposure of the right adrenal gland revealed a dark brown tumor which was removed. Pathological examination showed no malignancy. The boy recovered and growth and development were normal for the next 4 years. The breasts decreased slowly.

A 5-year old girl was studied at the same time. Over a period of 5 months pubic hair appeared and grew rapidly; the clitoris became enlarged, the voice deepened and acne appeared. Examination revealed a normal vagina, uterus and ovaries. The sudden onset and rapid progress of virilization suggested a virilizing tumor of the adrenal gland. Transperitoneal exploration revealed a tumor attached to the right adrenal by a pedicle which was removed. Examination of the tumor revealed malignancy. The virilizing symptoms receded somewhat but metastasis occurred and the patient died.

In one case, that of the girl, the hormone produced by the tumor behaved like an androgen; in the other like an estrogen, but no information was obtained

THE INTERSTITIAL TISSUE OF A HUMAN HERMAPHRODITE

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J. Clin. Endocrinol., 8: 271-274, 1948

The site of production of the sex hormone in human males is still a disputed question. Recently, there has been evidence presented which supports the contention that the sustentacular cells of the seminal tubules (so called cells of Sertoli) are the producers of the female sex hormones. Apparently, there is a neural relationship of the interstitial tissue in human sex glands, and the sympathicotrophic cells of Berger may be of an interstitial nature. Intimate connections between the interstitial cells of Leydig and nerve fibers have been found in both ovaries and testes. Since the interstitial cells of the testis and the theca interna of the ovary are homologous, a similar function might be expected to exist in these gonads. It has been suggested that the nervous stimuli might modify the normal secretion of the homologous elements so as to give rise to different hormones.

With these thoughts in mind, the authors restudied the sections of the gonad of a human hermaphrodite in search for clear-cut neuroepithelial complexes. Numerous incidences of intermingling of interstitial cells and amyelinic nerve fibers existed which were similar to the neuro-epithelial complexes observed in normal and cryptorchid males. The only apparent difference was the absence of vacuolization and inclusion bodies seen in the sympathicotrophic cells of normal males. The cytoplasm stained uniformly, which might be related to the low secretory activity of the cells.

These observations raise the question of the functional importance of the innervation of the interstitial cells. This case is suggestive of a degree of control of hormonal production and release by the autonomic nervous system.

(This is a praiseworthy effort to demonstrate the neuro-epithelial link-up which is believed to exist between the interstitial cells and the nervous system, just as a similar liaison is postulated in reference to various other endocrine structures, but it still leaves the problem unsolved. The homology of the theca interna cells of the ovary with the Leydig cells in the testis has recently been invoked in the explanation of certain masculinizing tumors of the ovary, although the evidence for this view is far from complete. During the preceding generation the luteinized theca interna cells were widely spoken of, especially in the German literature, as the interstitial cells of the human ovary, often forming large aggregations designated as the interstitial gland of the ovary (Interstitialdrüse). There was never any scientific evidence for this view, now generally abandoned. However, the anatomic homology of the theca interna cells, not necessarily only of the pregnant woman, may yet prove to be of significance, perhaps in the explanation of certain virilizing tumors of supposedly adrenal type, and those included under such designations as virilizing lipid cell tumors, hypernephroid tumors and masculinovoblastoma.

Thus far most of the evidence along this line has been largely morphological and reliance on morphology alone is likely to be hazardous. Only recently I was sent a section of ovary from an infant of one month, in which the theca interna cells were large and polyhedral, and

TISSUE LOCALIZATION AND EXCRETION ROUTES OF
RADIOACTIVE DIBROMESTRONE

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Am. J. Obst. & Gynec., 56: 260-268, 1948

The metabolism of steroids is a poorly understood subject, although the use of radioactive testosterone, progesterone and estrone could do a great deal to unlock the mysteries of steroid metabolism. However, up to the present time no such compounds have been synthesized. As a short cut, one of the steroids was treated with an artificially radioactive halogen, namely, bromine-82. It was thought that the brominated steroid might behave in a fashion sufficiently similar to that of the parent hormone so that conclusions could be drawn concerning selective absorption and routes and methods of metabolism. The steroid prepared was dibromestronone, which was only weakly estrogenic, if at all.

Dibromestronone was not selectively localized in the rabbit in the adrenals, spleen, ovary or testis. A high concentration occurred in the gall bladder within 6 hours after injection. It was not selectively localized in the liver, ovaries or uterus of the female monkey or in the uterus of the dog. Dibromestronone was largely excreted through the common bile duct into the intestine. From this organ it may be reabsorbed into the portal circulation, ultimately to find its way to the kidney and into the urine. It is probably excreted into the bile and into the urine largely as a conjugated phenolic steroid. The observations strongly support the theory of an enterohepatic circulation of dibromestronone and, by implication, of other steroids as well. If this is true, urinary assays of these substances, with respect to disease, become of little significance, unless the factors of hepatic and intestinal influence are considered. 2 figures.

(This interesting paper represents a praiseworthy effort to apply the new and still undeveloped method of radioactive isotopic study to the problem of the life history of the body steroids. That this problem is in need of clarification is recognized by all investigators. The authors themselves recognize the difficulties and uncertainties attached to their plan of attacking the problem, but even so, it is of interest that their work appears to substantiate the view that the liver, and probably also the enzymes and the motility of the small intestine, and possibly also, as they suggest, the flora of the large intestine, play vital parts in determining the urinary titers of hormone. The early enthusiasm concerning the significance of the urinary output of estrogens has been followed by disappointment and increasing skepticism, and on the whole I believe it may be fairly said that the practical yield of such urinary studies in the elucidation of clinical problems has been very unimpressive, and in many cases it has undoubtedly been misleading.—Ed.)

GRAFTED MOUSE OVARIES WITH THEIR ADRENAL CORTICAL FUNCTIONS

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Endocrinology, 42: 339-351, 1948

Ovaries were grafted into the ears of male mice, on the testes of male mice, and autografted into the ears of female mice in order to study the adrenal cortical function of the ovaries. After 2 weeks, all adrenal tissue was removed. A control group of completely adrenalectomized mice all died within 29 days.

In the experimental group of 108 females, 54 survived within the control period when adrenalectomized, and 35 survived an average of 121 days. Sixteen had the grafts removed and survived 38 days. Thirty-eight males with grafts on the testes showed 16 dying within the control period, 6 surviving 94 days, and 11 with excision of grafts surviving 44 days. Of 28 males with ear grafts, 17 died in the control period, 3 survived 56 days, and 4 with grafts removed survived 36 to 109 days.

The author concludes that mouse ovaries can maintain life in the host mouse after the removal of adrenal cortical tissue. Intact gonads or removal of gonads does not significantly alter time of survival. Removal of grafts in adrenalectomized mice resulted in death. No histological or chemical explanation is offered.

(The purpose of this study is to determine whether the previous grafting of the ovaries, as described by the author, will confer any degree of protection to the animals from subsequent adrenalectomy, the inevitable result of which is death within 29 days. The results seem to indicate that the lives of the animals are substantially prolonged, but why and how is not clear. While the adrenals appear to be at least a supplementary source of estrogens and certain progesterone-like hormones, no one, so far as I know, has demonstrated or even suggested that the gonads in turn take any part in the production of desoxycorticosterone or cortin. The hormonal interrelationships between the gonads and the adrenal cortex are still largely unknown, and, as I have previously remarked in these pages, the problem is rich in potentialities.—Ed.)

divided into groups separated by delicate trabeculae of fibrous tissue, so that they closely resembled the cells of the zona fasciculata of the adrenal cortex. Whether this histological resemblance has any significance, I am sure I do not know. For that matter, the nature of the undoubted relation between the adrenals and the gonads is still a closed book. To my mind, this particular problem offers as rich potentialities as any I can think of in the field of endocrine research.—Ed.)

THE ARREST OF ABNORMAL UTERINE BLEEDING WITH PITRESSIN TANNATE IN OIL

R. C. BENSON

Am. J. Obst. & Gynec., 55: 286-292, 1948

Pitressin, the vasopressor of the posterior pituitary, stimulates contractions in the not pregnant uterus acting as a mechanical tamponade to uterine bleeding. Thus its use as a uterine hemostatic agent to precede final curative therapy is suggested.

Pitressin tannate in oil (2.0 cc. or 10 pressor units) intramuscularly was employed as a single injection in 100 unselected gynecological patients suffering from menometrorrhagia of all types in an attempt to arrest uterine bleeding. Only cases of pelvic malignancy were excluded. Thirty-one of the cases ceased to bleed within 24 hours. In 48 hours 17% more stopped. Only 16% failed to note a checking.

Patients with gynecological causes or constitutional disease causing menometrorrhagia showed a better response than patients with pregnancy complications; but all groups benefited and no serious toxic effects were noted. 6 tables.

(The use of posterior pituitary preparations is not altogether new in the treatment of even functional uterine bleeding. In those happy days of yore, before the hormones had begun to bedevil us, I recall that one of my own favorite ways of treating functional bleeding was with the hypodermic employment of posterior pituitary extract—this, I believe, was before the latter was split up into its two constituent parts. And quite a number of patients were apparently improved, just as some were apparently improved by the even older ergot therapy. The word “apparently” is just as clearly indicated here as it is in the evaluation of our modern hormone treatments of the same disorder, although one does not have to be a wild-eyed ductless gland faddist to feel that genuine advances have been made in this field. It is surprising to read that Benson considers that his oxytocic form of therapy gives less satisfactory results with pregnancy complications, such as miscarriage, than in other forms of bleeding, including the constitutional group. My own impression would be just the opposite.—Ed.)

minutes until the pain was relieved. A mild jag is a pretty good anti-dysmenorrheic, though it should not be carelessly prescribed.

But the dashing cohorts of the then young Council on Pharmacy and Chemistry of the good old A.M.A. came charging to the rescue of deluded womankind, and their expert legal sharpshooters soon routed the shameless moneybaggers, with no audible plaudits from the ranks of the rescued maidens in distress.

And now, it seems, certain renegade scientists are able to show that viburnum really is a potent relaxant of smooth muscle, and thus becomes as eligible for study and consideration as an anti-dysmenorrheic as, for example, such élite endocrines as progesterone. For that matter, we poor clinicians would be grateful if the scientists could agree among themselves whether or not progesterone is a relaxant of uterine muscle.

The study of Diehl and Hundley leads them to conclude that viburnum prunifolium has no effect on uterine contractions at any phase of the cycle, whether painful or not. And we are right back to the \$64 question, What is the cause of primary dysmenorrhea? Is it really due to painful, colicky contractions of the uterus, as has been almost universally assumed, or is it due to some other more underlying factor, such as a disorder of the spiral arteriolar circulation of the uterus? Such a vascular factor has been suggested on hypothetical grounds, first by Schulze, for many years, long before anyone knew anything of the coiled arterioles. The problem is being envisaged in the studies of some of the investigators of the endometrial vascular mechanism, and it is not impossible that in some future day dysmenorrhea may be considered a vascular problem rather than one revolving about uterine muscle contractility.—Ed.)

INDUCTION OF UTERINE BLEEDING IN AMENORRHEA WITH A SINGLE INJECTION OF PRECIPITATE ESTRONE AND PROGESTERONE

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J. Clin. Endocrinol., 8: 406-412, 1948

A new method of treatment of amenorrhea with a single injection of estrone and progesterone is reported. Estrone and progesterone dissolved in an organic solvent are precipitated in the syringe by the addition of saline solution and injected intragluteally.

The doses required in primary amenorrhea are 5 to 10 mg. of estrone and 50 mg. of progesterone. Five patients received 8 treatments, of which 7 were successful.

The dose required for secondary amenorrhea is 5 mg. of estrone and 50 mg. of progesterone in the first treatment, but in subsequent treatments the amount of progesterone may be reduced to 25 mg., or 50 mg. of progesterone without estrone may be given. This may indicate that the body has been rendered more sensitive to the hormone. Twenty-nine patients received 43 treatments and 40 were successful.

Three to 4 treatments at monthly intervals are given and then spontaneous

THE MENSTRUAL CYCLE

THE ROLE OF UTERINE MOTILITY IN ESSENTIAL DYSMENORRHEA

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Am. J. Obst. & Gynec., 56: 281-290, 1948

In this study the authors concerned themselves primarily with the effects of the glucosides of viburnum on primary dysmenorrhea. The clinical and experimental effects of this drug were tested. Three groups of patients with dysmenorrhea were treated with viburnum. An attempt was made to demonstrate clearly the absence of all other causes of dysmenorrhea, but this was not always possible because of the type of patients treated.

The first group of cases were seen in the gynecologic dispensary and consisted primarily of Negro women. The second group were women at a large industrial plant where the drug was administered by a nurse on a symptomatic basis. In the large combined group the results were clinically disappointing, and only about 55 per cent of the cases obtained satisfactory relief of pain.

An attempt was made to correlate these findings with the pharmacological action of viburnum prunifolium which experimentally is a potent smooth muscle relaxant. For this purpose an intrauterine bag was devised to record the effects of the drug on the intact uterus. Fifty-three patients were studied in this manner. Twenty-nine of these patients suffered from varying degrees of dysmenorrhea and the remaining 24 were free from menstrual discomfort. A careful study of these patients revealed no significant difference in any component of contraction between those patients suffering with dysmenorrhea and those free from menstrual pain. In addition, viburnum prunifolium and its crystalline glucoside do not appreciably alter the contractions of the intact human uterus either during the actual process of menstruation, painful or otherwise, or during the portion of the normal menstrual cycle influenced by estrogen or progesterone. The authors conclude that any relief obtained is on a basis other than muscle relaxation.

(The ups and downs of various drugs in the history of pharmacology and therapeutics are well illustrated in the case of viburnum prunifolium. Every old practitioner will remember the days when that good old proprietary known as "Hayden's Viburnum Compound" was the sovereign lay remedy for menstrual cramps, and many other "female disorders," so that it seemed that many millions of women, like the proverbial 40 million Frenchmen, could not be wrong. The learned medical profession quite naturally ridiculed and resented this patent medicine, emphasizing the utter inertness of its chief ingredient, viburnum prunifolium. The more realistic among them did not dispute the frequent effectiveness of the nostrum, since it contained, as I recall it, something like 40 or 50 per cent of alcohol, and the prescribed dose, if my aging memory can still be trusted, was a tablespoonful every 10 or 15

and one is justified in assuming that sooner or later, if other factors are normal, the jackpot is hit—and it is usually not long. With women who have very irregular cycles, in whom it is more difficult to figure out optimum phases, there is more advantage to be hoped for from basal temperature readings.

If I read Farris's paper correctly, his "prediction" of the day of ovulation is based on the shaky premise that the day of ovulation shows only minor variations in consecutive months. This is certainly not the usual concept, and it seems to me that a far larger number of observations than those reported by the author is necessary to justify such an assumption. Wouldn't it be nice if each woman had her own characteristic ovulation day, so that a coital timing mechanism could be worked out? Whether even this would add greatly to results is not certain. I personally have always felt that if a normally menstruating woman has been shown by biopsy to be ovulating, and if she is given advice as to the optimum phase for fertilization, some other factor than mere timing is responsible if conception does not occur.—Ed.)

MEPRANE IN THE TREATMENT OF THE MENOPAUSAL SYNDROME

AN EVALUATION OF ESTROGENIC EFFICIENCY AND TOXICITY

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Am. J. Obst. & Gynec., 56: 541-548, 1948

The authors report the results of an evaluation of Meprane in the treatment of 45 menopausal patients followed from 2 to 12 months. This evaluation was accomplished by observing the effect on cornification of vaginal smears, by urinalysis, by hematologic and blood chemistry studies, by repeated physical examinations and by direct questioning of the patients at frequent intervals.

Meprane was found to cornify vaginal smears effectively, the maximum effect being evident in about 4 weeks. Full cornification required a dosage of from 3.0 to 5.0 mg. per day. Better symptomatic responses were obtained from lower maintenance dosages when full cornification had been established.

No chronic toxic manifestations resulting from therapy were noted and no sensitization to Meprane occurred. Side effects were not common.

The tentative impressions gained were that Meprane is a highly effective agent in the control and alleviation of menopausal symptoms. The writers add a plea to evaluate every menopausal patient as a whole, searching for other causes of symptoms than the menopausal syndrome alone.

(Meprane is a good estrogenic preparation, and so are a good many other oral estrogens now readily available. For that matter, stilbestrol is an excellent oral estrogen and cheaper than the others. Many gynecologists, therefore, use one or the other of substances like meprane, estinyl hexestrol, benzestrol, dienestrol, etc., chiefly in the 10 to 15 per cent of women who can not take stilbestrol.—Ed.)

bleeding is awaited. This spontaneous monthly bleeding, without hormone administration, occurred in 5 patients with primary amenorrhea and in one with secondary amenorrhea. It is suggested that perhaps the treatment provides stimulation of gonadotrophic hormones in the anterior pituitary.

Advantages of this method of treatment are: (1) one injection is required, which is of psychological importance to the patient; (2) pituitary action is not inhibited by small doses of the estrogenic hormones; and (3) the injections are well tolerated.

(The plan described by the authors is a modification of the one suggested by the senior author some years ago. There is no doubt that the injection of progesterone, according to the original plan, will often induce bleeding, but in a large proportion of cases this is not followed by recurring menstruation, though the still meager reports on this point show considerable variation. In any event, the results have not been sufficiently striking to lead to any very wide adoption of the method. Whether the revised plan, as described in the present paper, will yield definitely more impressive results remains to be seen.—Ed.)

THE PREDICTION OF THE DAY OF HUMAN OVULATION BY THE RAT TEST AS CONFIRMED BY FIFTY CONCEPTIONS

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Am. J. Obst. & Gynec., 56: 347-352, 1948

The author performed a series of 208 tests on 46 individuals in order to determine the exact time of ovulation. The occurrence of human ovulation was detected by the reaction of the immature rat's ovary to the hypodermic injection of the urine of the subject. The day of ovulation ranged from the sixth to the twentieth day of the cycle, with 54 per cent occurring on cycle days 11 to 13 inclusively. The postovulatory phase averaged 14.8 days, with a range of 11.5 to 20 days.

By observing the time of ovulation over a period of several months, the day of ovulation could be predicted with some accuracy in subsequent months. The rat test was performed prior to sexual intercourse or insemination so that the exact day of ovulation could be determined. Using this plan, 50 conceptions occurred in 46 patients.

(I have of course had no personal experience with the author's method of predicting ovulation, but I am frank to say that I can not see how it could ever prove to be a widely applicable addition to methods of managing sterility. As a matter of fact, even the far simpler method of basal temperature readings, with due allowance for possible inaccuracies, has always seemed to me to be of limited value in women with essentially normal cycles, since all such studies have merely confirmed the results of histological investigations which show a definite ovulation span. A part of the management of sterility cases, therefore, has always been the advice to have coitus as frequently as possible during the optimum phase,

THE CAUSE OF PHYSIOLOGIC BASAL TEMPERATURE CHANGES
IN WOMEN

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J. Clin. Endocrinol., 8: 550-563, 1948

The authors felt that the rise in basal body temperature during the luteal phase of the normal ovarian cycle is brought about by progesterone elaborated by the corpus luteum. The artificial reproduction of the normal hormonal cycle by the substitution of estrogens and progestins resulted in a temperature curve simulating that of the natural ovarian cycle. Progesterone can be identified as the factor responsible for the rise and maintenance of the elevated temperature in the luteal phase of the cycle. A close parallel was noted between the excretion of pregnanediol, the development of the corpus luteum and the changes in basal body temperature. With the rise in temperature there is an increased output of pregnanediol. The only outstanding difference in women with artificially produced cycles was that the rise of basal temperature at the onset of progesterone therapy was more rapid and the decline more prolonged. The normal corpus luteum probably liberates progesterone more slowly and the amount of secretory activity varies with individuals.

The ovarian function following the surgical removal of the uterus was also studied by the use of basal temperature graphs. The general pattern of the curves was typical of normal ovarian activity, and progesterone activity, as measured by the urinary output of pregnanediol during a 24-hour period, was not altered. It was concluded that follicles grow to maturity, rupture, and become functional corpora lutea which have a normal life cycle even in the absence of the uterus. In the human, the uterus is not necessary for a normal hormonal cycle.

Ovulation in many, if not in most instances, occurs with the rise in temperature rather than at the lowest point prior to the rise. It is probable that follicle luteinization begins in the theca interna cells during the stage of rapid growth just prior to ovulation and becomes accelerated with the rupture of the follicle. This explanation would account for the onset of the rise in basal body temperature prior to ovulation. 8 figures.

(See comment on following abstract.—Ed.)

RELATION OF INTERMENSTRUAL SYMPTOMS AND SIGNS TO OVULATION AS DETERMINED BY BASAL BODY TEMPERATURES

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Am. J. Obst. & Gynec., 56: 537-540, 1948

Little attempt has previously been made to use the basal body temperature to correlate signs and symptoms of ovulation. Zuck observed 248 menstrual periods and found significant symptoms during the midinterval among 50 per cent of the patients married, menstruating and otherwise stable. Palmer and DeVillers, in a study of 75 gynecologic patients, found that in those patients who apparently ovulated they associated pain, spotting, leucorrhea and mastalgia.

For the present study, 20 healthy women, aged 19 to 31 years, kept menstrual records and basal body temperature records for prolonged periods of time. All but one woman gave evidence of ovulation at least once while under study, and three-fourths of the women had one or more anovulatory cycles. One-fifth of the ovulatory cycles were accompanied by abdominal pain, while none of those with monophasic temperature records suffered discomfort. Intermenstrual spotting was significant for only one woman; the other patients either had none or else the relationship was too indefinite to be of value. Likewise, physiologic leucorrhea and mastalgia did not seem to bear any relation of significance to ovulation. There are women, the author states, who, without physical or anatomic reason, do not appear to ovulate. Kamman has good evidence to indicate that emotional disturbances can reflect themselves in endocrine dysfunction and interfere with ovulation.

(A useful correlative study, although the series is small. I believe that most gynecologists, on the basis of routine gynecological histories of their own patients, would estimate that only a comparatively small proportion of women fly any sort of a symptomatic flag, in the form of abdominal discomfort or pain, at the time of ovulation. On the other hand, it is quite probable that intensive interrogation on this point might show a considerably larger incidence, and it is this sort of intensive study which is reported by the author on 20 women. At times, of course, this ovulation pain or mittelschmerz may be intense, and I have seen a few cases in which its occurrence was anything but a help to the woman anxious to conceive, since the severity of the pain made her abstain from coitus at this presumably favorable time. I do not believe that many would agree with Zuck, quoted by the author as saying that 50 per cent of patients show significant midinterval symptoms.—Ed.)

VULVA AND VAGINA

VAGINAL AND RECTAL PRURITUS—ETIOLOGY AND TREATMENT

E. L. CORNELL

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Am. J. Obst. & Gynec. 55: 691-698, 1948

It is the author's opinion that vaginal and rectal itching is a neglected field in medicine. There is always a reason for such symptoms and study of each case will reveal the etiology.

Vaginal itching or burning is most often due to *Trichomonas vaginalis* which can be difficult to cure. The physician should adopt one method and use it systematically until it is certain that this will not benefit the individual patient. The author's procedure is to have the patient insert one Devegan tablet nightly and to report for cleansing of the vagina and the insertion of 3 tablets on the 1st, 3rd, and 5th day of the period for 4 periods. He feels that douches are useless and are likely to cause reinfection. If a week after the fourth period the secretions are negative, the patient is cured. The possibility of reinfection from the sexual partner must be considered. It is best to warn patients that trichomonas vaginalis is difficult to clear up. In pregnant women the disease is incurable.

Thrush is the second greatest cause of vaginal itching. A membranous yellow discharge occurs in which monilia are present. Treatment by tampons soaked in 2 drams sodium borate dissolved in glycerine is effective. The tampons are used 4 days and the patients examined after a week. During pregnancy thrush does not respond to treatment but discomfort can be alleviated by use of gentian violet or sodium borate suppositories.

Colon bacillus may infect the urinary tract or the vagina as a result of improper wiping or douching. Diagnosis is made by culture or smear and treatment by sulfathiazole is effective.

Other types of bacterial infection causing burning or itching are; staphylococcus, streptococcus and gonococcus. Pain is nearly always present and except in cases of gonococcus the source of the infection is difficult to ascertain. The sulfonamides and penicillin are used in treatment. Vaginitis as the result of the use of cauterizing drugs is seen occasionally. Some patients are allergic to gentian violet, brilliant green, etc. Senile vaginitis can cause burning and itching also and is sometimes helped by the use of oral estrogens.

There are many external causes of itching. Leucoderma, which appears with painful cracking of the mucous membranes and skin, responds to gentian violet therapy. Trichophyton, where patient has athlete's foot, is a source of infection causing itching too. Lesions here may be extensive and here, too, gentian violet can be used. Itching may be due to lack of cleanliness and improve with daily washing.

HORMONAL FACTORS INVOLVED IN THE REGULATION OF BASAL BODY TEMPERATURE DURING THE MENSTRUAL CYCLE AND PREGNANCY

C. L. BUXTON AND W. B. ATKINSON

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J. Clin. Endocrinol., 8: 544-549, 1948

It is the purpose of this paper first, to present evidence as to the actual cause of the basal body temperature rise during the latter half of the menstrual cycle and second, to investigate the progress of the basal body temperature throughout pregnancy.

For the former purpose, 6 patients with secondary amenorrhea and with little or no endometrial activity as determined by biopsy, were studied in the following manner. After a temperature base line had been established, the patients were given orally a priming dose of estrogen of 3 to 5 mg. of either estrone sulfate or diethylstilbestrol daily for about 2 weeks. Progesterone, in amounts varying from 10 to 25 mg. daily, was then administered for from 7 to 14 days. During this time, estrogen was either discontinued or maintained at half the original dosage. The temperature curves obtained from these patients during treatment showed that estrogen may produce a slight depression of basal body temperature whereas progesterone, with or without estrogen, produces a very definite rise. Biopsies revealed that characteristic endometrial responses to the hormones took place.

The postovulatory temperature rise was also maintained and menstruation postponed 10 to 30 days in normal women by the administration of chorionic gonadotrophin. However, chorionic gonadotrophin administered to a castrate following estrogen priming did not result in any significant change in basal temperature. It was therefore assumed that the maintenance of the postovulatory temperature rise by chorionic gonadotrophin was due to its luteotropic effect, and that here also progesterone produced the temperature response.

To determine whether the temperature rises were maintained throughout gestation, 3 women (one through 2 pregnancies) kept temperature charts until delivery. The temperature fell to its preovulatory level uniformly between the fourth and fifth month in all cases. This was in spite of the commonly supposed steady rise in progesterone activity as determined by pregnanediol excretion.

Several possibilities are discussed to account for the above discrepancy, but no final explanation is offered. One possibility is that a refractory state develops in connection with the thermogenic action of progesterone. Another is that the lytic activity of the trophoblast on the decidual tissue of the mother during the early months of pregnancy results in a slight febrile reaction on the part of the mother. An additional explanation might be that the decline of the elevated basal temperature at midpregnancy is consistent with a hypothetical decline of active circulating progesterone. Further work is indicated to settle this question. 6 figures.

(The whole question of basal body temperature records is fully discussed in the Collective Review of the subject by Allan Palmer in this issue of the Survey.—Ed.)

Recently, Plastigut, a plastic-incorporated, non-reacting, non-absorbable suture, has been used with good results. (5) Postoperative care.—An indwelling catheter, sutured to the labia, is placed in the bladder and left in for 14 to 16 days to prevent bladder tension from accumulation of urine. Prophylactic doses of sulfadiazine are advised during the period of catheterization.

The author reports the case of a 64-year-old woman who had been operated on for carcinoma of the cervix by the Percy-Wertheim operation in which the Percy cautery was used. A fairly high vesicovaginal fistula resulted. This was repaired according to the technic described above. Following operation, the patient experienced 4 months of complete freedom from leakage, until during an examination, the writer noted the presence of a suture at the site of repair. In attempting to remove it, the author caused a recurrence of leakage, and a second operation was necessary. This was successful, the patient having had no urinary incontinence to date. The author states that he has learned a bitter lesson resulting from thoughtless interference, and is not likely to repeat the same performance. 4 figures.

(The 5 factors set forth by the author are well chosen, although there will of course be variations in individual practice concerning No. 3, dealing with the technical details of the operation. Moreover, I feel quite sure that the author himself will agree that the operation must depend on such factors as the location and the size of fistula. Undoubtedly the procedure he describes would fit many cases, while in many easily accessible fistulas of not too large size, the classical Sims operation, using silver wire for suture, is highly successful. On the other hand, in the larger fistulas it seems to me that no procedure gives as satisfactory results as free mobilization of the bladder, so that the opening in the bladder can be sutured without lesion like any bladder wound, followed by approximation of the vaginal flap in such a manner as to avoid overlapping of the vesical and vaginal lines of sutures. Catgut as a suture material gives excellent results if the sutures are properly placed, though there is certainly no objection to silver wire for the vaginal wound for its greater splinting effect. The possibility of opening up the bladder by too rough removal of sutures is properly emphasized, as is the greatly improved exposure made possible by the Schuchardt incision in otherwise inaccessible fistulas in the vaginal vault.—Ed.)

MALIGNANCY OF THE VULVA

J. A. BROWN

Regina, Sask.

Canad. M. A. J., 58: 181-183, 1948

The author divides malignancies of the vulva into the following groups: epidermoid carcinoma, vestibular carcinoma, Bartholin gland carcinoma, clitoris gland carcinoma and hidradenoma carcinomatorum. By far the most common type of carcinoma of the vulva is that which originates from the epidermis, and the common sites are the labia and prepuce of the clitoris. In a large majority of patients a predisposing factor in the development of a cancerous growth is a

Rectal itching may be caused by ameba or other intestinal organisms which must be cleared up in order to prevent itching. Fungus growth and uncleanness are two other causes of rectal itching.

(This paper, by a gynecologist of many years' experience, is of considerable practical importance, dealing as it does with the management of a frequent and troublesome gynecological symptom. While itching is common with trichomonas vaginalis, the latter has been so widely discussed for many years that it is not likely to be overlooked by any reasonably competent gynecologist or even general practitioner. As a matter of fact, the value of Cornell's paper is that he calls attention to the many other possible causes of pruritus, with suggestions as to their management. On the latter point, there will naturally be individual preferences for one form of treatment or another. For example, in the treatment of senile vaginitis, I prefer the vaginal suppository method of estrogen therapy to the oral. The detection of the cause of troublesome pruritus is not always easy, but it is worth the effort, for no group of patients is more grateful than those who can be relieved of this pesky symptom.—Ed.)

VESICOVAGINAL FISTULA

J. E. BELLAS

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Illinois M. J., 93: 138-143, 1948

As a result of numerous experiences in the repair of vesicovaginal fistulas, certain factors have impressed the author as being of considerable importance. The application of these details often may determine whether the operation is a success or a failure. Five factors are listed: (1) Time of operation.—The patient should be prepared to her optimum physical state, and sufficient time must elapse to permit the tissues adjacent to the vesicovaginal fistula to regain their normal vitality. (2) Adequate exposure.—High fistulae require much freer exposure than those located low. Also, one often encounters a contracted or constricted vaginal canal or vaginal vault, wherein the best exposure can be obtained by utilizing the Schuchardt incision. (3) Technical details of operation.—A vaginal mucous membrane collar is created by circular incision around the margins of the fistula. The edges of this collar are then moderately undermined toward the fistula to permit later infolding. The edges beyond the circular incision are then undermined laterally as far as possible. It is particularly important to sever the numerous scar bands and strands that are present subjacent to the vaginal mucosa. This exposes the paravaginal connective tissue, the suture of which is of prime importance in the repair of the fistula. The vaginal collar may be dealt with by bringing the vaginal edges toward the bladder by a strand drawn through the urethra and followed by the application of 2 to 3 overlying purse-string sutures. (4) Choice of suture.—In the writer's experience, a certain proportion of cases repaired with catgut failed to heal on primary intention.

ASPECTS IN THE TREATMENT OF VULVAR AND CERVICAL CARCINOMA

GRACE C. DONNELLY WITH W. A. G. BAULD

Royal Victoria Montreal Maternity Hospital and McGill University, Montreal, Que.

Am. J. Obst. & Gynec., 56: 494-501, 1948

A survey of female pelvic malignancies treated in the authors' Clinic from 1926 to 1945, inclusive, revealed 40 cases of carcinoma of the vulva, 664 cases of carcinoma of the cervix, 177 cases of carcinoma of the uterus and 185 of carcinoma of the ovary. In this paper, the vulvar and cervical malignancies are discussed.

Local recurrences of carcinoma of the vulva, particularly after vulvectomy, have been few. However, subsequent inguinal gland metastases have not been infrequent. Treatment of the inguinal glands, either by surgery as recommended by Taussig, or by x-ray as is now being done in this Clinic, would appear to be important in the initial treatment of carcinoma of the vulva.

The incidence of cervical stump carcinoma to cases of carcinoma of the cervix is 6.02 per cent, and to the number of subtotal hysterectomies, 1.75 per cent. Of 28 patients with true cervical stump carcinoma, 39 per cent were known to have had bilateral oophorectomy with the subtotal hysterectomy; this fairly large percentage does not support the theory that carcinoma of the cervix is related to ovarian stimulation. There were no Stage I cases of true cervical stump carcinoma, and the majority were in Stages III and IV. These figures suggest that the patient may develop a false sense of security following operation and be more prone to disregard subsequent symptoms.

Though surgical treatment for carcinoma of the cervix has not been practiced in this Clinic, there has been a small group of 37 patients for whom the procedure of radiation followed by surgery has been used. Of these 37 patients, 12 were in Stage I, 13 in Stage II, and 12 in Stage III. Most of the patients were treated by radium and panhysterectomy; the upper vagina was left and there was no dissection or extirpation of glands or other pelvic structures. Of the 37 patients, 14, or 37.7 per cent, were living and well 10 years after treatment.

(See comment on preceding abstract of paper by Brown. I believe that many gynecologists, like the authors of this paper, have been struck with the comparative infrequency of local recurrences after thorough vulvectomy, even in advanced cases which later go on to death from intrapelvic gland metastases. As a matter of fact, one occasionally sees cases of this sort in which neither local nor regional recurrence occurs, as I have mentioned in previous comments on this subject.

The authors' report of results in the radiation therapy of cervical stump cancer are good. They bear out the views expressed by Behney and others that this form of cancer, contrary to earlier views, is certainly no less favorable than cervical cancer in general. The fact that 39 per cent of 28 cases of stump cancers had had bilateral oophorectomy with the supravaginal hysterectomy leads the authors to state that this percentage does not support the theory that cervical cancer is related to ovarian stimulation. However, this would apply only to the actual production of cancer by estrogens, for which there is little evidence. It would

leukoplakia vulvitis, with or without kraurosis. In general, enlargement of lymph nodes is not a reliable index to metastasis, and extensive dissection of local nodes is necessary to effect a permanent cure.

Treatment of these cases must in the first instance be preventive and the author feels that leukoplakia, senile warts and cystic enlargement of Bartholin's gland demand immediate and often radical attention. Treatment of the cancer is best conducted by a combination of surgery and radiation. Radiation alone is usually unsatisfactory, as the metastases are rarely destroyed by such therapy and the skin of the vulva does not tolerate radiation satisfactorily. In the author's series, a modified Basset operation was followed by x-ray irradiation.

Thirty-six cases were studied, 27 occurring on the labium majus and 3 on the labium minus. The age of the patients ranged from 45 to 75 years, with the greatest proportion in the groups from 55 to 65 years. Twenty-one cases received radical vulvectomy, bilateral-gland and post-operative radiation. Radical vulvectomy with bilateral gland dissection was performed in 2 cases. Four patients had radical vulvectomy and radiation to the gland area, 6 cases received radiation alone and 3 cases refused treatment.

The tumors were classified in 5 groups with group 1 representing small tumors without metastasis and group 5 showing far advanced tumors with broken down lymph glands and cachexia. Twelve of 13 cases in group 1 are alive; 6 of 8 cases in group 2 are living, and 3 of 8 cases in group 3 are alive. All cases (7) in groups 4 and 5 are dead.

(I do not like the classification of vulvar carcinoma suggested by the author. Vestibular carcinoma, clitoris carcinoma and for that matter many carcinomas of the Bartholin gland are just as epidermoid as carcinoma of the labia. Since adenocarcinoma of the Bartholin gland also occurs, there are some who might prefer to segregate this as a special form, even though the Bartholin glands are integral parts of the vulva. Hidradenoma is a perfectly benign lesion and its occurrence is not limited to the actual vulvar region, so that it has no proper place in the category of vulvar carcinoma. So far as I know, in only one case, that of Eichenberg, has adenocarcinomatous change been demonstrated, and I see no advantage in complicating the classification of vulvar carcinoma by envisaging this case in a group to be called hidradenoma carcinomatorum.

The results of the treatment in the cases reported by the author are amazingly good, making allowance for the advanced cases in his groups 4 and 5, in which no one would expect good results. They appear to substantiate the prevailing popularity of the Basset type of radical operation when this is feasible. I presume that the bilateral gland dissection which the author performed in addition to vulvectomy refers to this type of operation rather than to bilateral inguinal adenectomy alone. In recent years, however, a number of reports have appeared which showed surprisingly good results from much less extensive procedures which many surgeons would consider inadequate, so that the statistical review of this question may leave one a bit confused.—Ed.)

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not have much bearing on the more timely but still disputed question of whether cancer growth could be accelerated by the estrogens present in the circulation of women during reproductive life, or, to put it practically, whether the growth of cancer in such estrogen-dominated organs as the breast can be retarded by castration or by radiological abolition of ovarian function.—Ed.)

PRIMARY CARCINOMA OF BARTHOLIN'S GLAND

R. J. CROSSEN

Am. J. Surg., 75: 597-600, 1948

A report is made of Bartholin carcinoma in a 64-year-old patient. In 1941, the patient received deep x-ray therapy for adenocarcinoma of the endometrium, and a complete hysterectomy was done. In April, 1944, the patient appeared with the complaint of vulvar itching of a month's duration. A solid growth about $\frac{1}{2}$ -inch in diameter was found at the right vulvovaginal gland. There was a small ulcerated area and the mass was partially movable. No evidence of recurrence of the uterine carcinoma was seen. A complete vulvectomy was done and the patient, when last seen in November, 1947, showed no evidence of recurrence.

A review of the statistics from large clinics shows that carcinoma of the vulva comprises 3 to 5 per cent of all carcinomas of the female genital tract. Carcinoma of Bartholin's gland occurs in 2 to 3 per cent of all vulvar carcinomas. The diagnosis is frequently missed preoperatively. Honan's 4 diagnostic criteria are: typical vulva site; deep in the labia; connection with the gland duct; and presence of intact gland tissue. Of the 88 cases reported in the literature, Bartholin's gland carcinoma was found to occur most often between the ages of 40 and 60 years. The signs and symptoms most frequently encountered were: a tumor, cystic and sometimes painful; an abscess or draining sinus; and swelling with soreness or itching. Treatment varied from wide excision, vulvectomy, vulvectomy with gland excision, radiation therapy with either radium or x-ray, or a combination of any of these treatments. No conclusions can be drawn in regard to prognosis because of the small number of patients involved.

(Primary carcinoma of Bartholin's gland is most frequently of the type of adenocarcinoma, although epidermoid cancer may also occur. Although the type is not mentioned in the above abstract, I presume it was adenocarcinoma. If this is so, I wonder how it was possible with a history of previous adenocarcinoma of the endometrium, even 6 years afterwards, to exclude the secondary nature of the Bartholin gland growth. Such extension can occur, just as it may occur to the vagina. Only recently, in a patient who had had a previous hysterectomy for adenocarcinoma of the endometrium, I observed several nodular metastases just within the introitus, practically at the vulva.—Ed.)

THE UTERUS

ENDOMETRIAL GROWTH IN MONKEYS

F. L. HISAW

Harvard University, Boston, Mass.

Science, 107: 457-458, 1946

The growth response induced in the uterine endometrium of castrated monkeys by chronic treatment with estrogen is limited, and reaches its maximum at 30 days. If, however, progesterone is given concurrently, the rate of growth is greatly increased and continues for a longer period. If the muscularis is cut, an endometrial mass will form in the celom which equals the size of the uterus.

Endometrial growth produced by estrogen in a uterine fistula is no greater than in an intact uterus. If progesterone is given concurrently, tongues of endometrial tissue will grow out through the fistular opening. The endometria of uteri that have been exteriorized through the abdominal wall and incised transversely from fundus to cervix show similar growth responses.

(The author of this paper has made many important contributions in the field of reproductive physiology. His most recent interest has been in the study of endometrial growth, as is seen in the condensed preliminary publication abstracted above. Dr. Hisaw was the guest of honor at the 1948 meeting of the American Gynecological Society, and his scholarly address on that occasion was devoted to a complete review of his experimental work on endometrial growth, with a discussion of the important conclusions he was able to draw. This paper, with many excellent illustrations, will appear in the near future in the American Journal of Obstetrics and Gynecology, and will be commented upon on its publication. As will be evident even from the above brief abstract, he has shown that, while estrogen is the growth hormone of the endometrium, its capacity in this respect is a restricted one, and it can be greatly enhanced by the concurrent administration of progesterone. But more anon!--Ed.)

THE ETIOLOGY OF FIBROMYOMATA OF THE UTERUS

PART I: A REVIEW OF THE LITERATURE AND PRELIMINARY COMMENTS ON THE HARTMAN-LITTRELL TECHNIQUE OF ASSAY

J. P. MARTIN

Howard University College of Medicine, Washington, D. C.

J. Nat. M. A., 40: 49-58, 1948

Throughout the ages, since Soranus of Ephesus first recognized the uterine myoma in the second century A. D., innumerable speculations and theories

not have much bearing on the more timely but still disputed question of whether cancer growth could be accelerated by the estrogens present in the circulation of women during reproductive life, or, to put it practically, whether the growth of cancer in such estrogen-dominated organs as the breast can be retarded by castration or by radiological abolition of ovarian function.—Ed.)

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The author discusses the ovarian hormone itself and lists some of the best methods of studying estrogenic levels in females. These methods are analyzed. The original method of Hartman and Littrell has recently been modified (*Endocrinol.*, 39: 120, 1946) using immature guinea pigs. If this technique is proved accurate in other hands, it may be best used to further investigations of the estrogenic etiology of myomas. It remains to be satisfactorily shown how the levels of fibroid-bearing women compare with nonfibroid-bearing women in the same age group. Other angles of approach would be the use of the Hartman-Littrell technique to find out if there is any essential difference in hormonal levels in women of different races, geographic areas and with selected types of pelvic infection.

(This is an interesting but not sufficiently critical resumé of the subject, particularly as it bears on the subject of the hormonal factor. For example, the author's allusion to the experimental fibroids produced in guinea pigs obviously has reference to the work of Lipschütz and his collaborators, but, as Martin does not make clear, these tumors are fibromas and not myomas, and they occur not in the uterine musculature but in any of the connective tissues of the pelvis and abdomen, even tissues far removed from the pelvis, such as in the gastrohepatic omentum. Moreover, the growths are not real tumors, since they regress after cessation of estrogen administration, especially if progesterone is given, and since they do not develop if estrogen and progesterone are given together. It is unfortunate that this work, important as it is, has so often been wrongly adduced to support the theory of estrogen origin of uterine myoma. So far as I know, only one small genuine myoma has been found in animals treated for a long time with estrogens, and in view of the large number of studies of this sort which have been made, this single instance is more likely to have represented a coincidental spontaneous myomatous nodule.

No one will deny that hyperplasia of the endometrium is estrogen induced, and there is far more logic in the theory that adenomyosis, rather than myoma, may represent the individual response of certain uteri to the ovarian hormones. In this condition, the growth propensities of the endometrium are manifested by a peculiar benign type of invasion into the musculature, while the latter itself undergoes marked hyperplastic changes. But, attractive as this theory is as applied to adenomyosis, we have no direct experimental evidence to substantiate it. As regards myoma, both the rationale and the evidence are even less.—Ed.)

EXPERIMENTAL ENDOMETRIOSIS

J. M. RAID

New York, N. Y.

Am. J. Path., 24: 726, 1948

"This problem was undertaken for the purpose of learning something about the pathogenesis of endometriosis. Forty rabbits were used. Pieces of endometrium were excised and then implanted in the skin, peritoneal cavity, ovary, and the anterior chamber of the eye. Some of the animals subsequently received injections of estrogens and of urine from pregnant women. After

have been advanced to explain its etiology. None has been completely satisfactory. Galen and Soranus stated that chronic irritation was the causative agent, and Virchow agreed with this view. It was later shown that even severe irritation caused only a simple diffuse hyperplasia and had no myoma-inducing effect on the myometrium, and it is an accepted fact that myomata do arise from the uterine musculature itself.

Various later authors proposed that hyperemia was the prime initiating factor, and beliefs ranging from excessive sexual activity to inhibited sexuality and dyspareunia were advanced as possible causes. Later still, well-nourished women of the upper classes were thought more prone to develop fibroids because of an assumed richer blood supply to the pelvis.

Albrecht theorized that isolated areas of the non-pregnant dormant uterine musculature shook off their state of rest and grew until their power of reproduction was exhausted, but the stimulus for this sudden change was not identified.

Meyer felt that the well-known regression of fibroids following the menopause was a result of general uterine atrophy and diminution of blood supply, due to loss of trophic stimulation of the uterine muscle by the ovary and not caused by a direct action on the tumor itself by the ovary. Moreover, it has been shown that those myomas which maintain their blood supply after the menopause may continue to enlarge.

The hormonal theory is a relatively new one, and much more investigation is necessary before it can be either accepted or rejected. Moench, in 1929, was the first to propose excessive hormonal stimulation allied with localized pelvic congestion as the cause of fibroids. Witherspoon, in 1933, stated that whereas endometrial hyperplasia resulted from short-duration hyperstimulation of the endometrium, fibroids resulted from long-duration hyperstimulation of the myometrium, and that hyperestrinism was the cause of this stimulation in both conditions.

The case for hyperplasia was settled by both animal experimentation and clinical data. However, some doubt concerning the relationship between endometrial hyperplasia and uterine myomas as to common etiology has been raised by both Brewer and Jones and by Henderson. Brewer and Jones, in their study of corpora lutea and the endometria of patients with uterine fibroids, found that the ovarian and endometrial relationships were not significantly altered in the cycles observed, nor was there evidence of excessive or unopposed estrogenic stimulation. Henderson found endometrial hyperplasia in only 6.5 per cent of a series of 727 cases of uterine fibroids. Certainly, if the two conditions have similar etiologies, there should be a closer correlation between them.

Experimental fibroids have been produced in guinea pigs by prolonged administration of estrogens, and prevention and even regression of the tumors has been brought about by the use of progesterone and testosterone. However, the experimental tumors, although allied, are perhaps not analogous to human fibroids. In the experimental tumor there is much less order of arrangement, particularly that of the fibrous tissue. Another important difference is the abundance of fibroblasts near the capsule in the experimental tumor.

2 months bleeding had been more or less continuous. Vesiculated masses of chorionic tissue protruded from the cervix. A careful curettage was performed. Microscopic examination revealed hydatidiform mole. A Friedman test 8 days postoperatively was positive.

Bleeding continued and 3 weeks later the entire uterus and adnexa were removed. A hemorrhagic lesion was found in the fundus of the uterus. Microscopic examination of this tumor revealed large acidophile, mono- and polynuclear cells of epithelial character that had infiltrated the uterine musculature. The resemblance of these cells to the syncytial cells of the chorionic villi establishes this tumor as a chorioma.

The authors state that, since these tumors are rare, they can best clarify the problem of choriomata by making their material available to those interested. Invaluable knowledge may result from a concerted attack on malignancy through choriomata, for nowhere are the physiologic and pathologic so closely intertwined. 1 figure.

(So far as I know, no one has reported a case of unquestionable chorionepithelioma made up only of syncytium, without Langhans cells, nor do I know of any case in which, as Reis and DeCosta say, metastases have been reported except locally in the vagina. Even if more distant metastases were reported, one could still doubt their histological malignancy, since even the trophoblast of benign moles, or for that matter, the trophoblast of normal pregnancy, may be deported to the lungs.

I mention these things because it has always seemed to me that Marchand, to whom we are so indebted for much of our knowledge of such placental lesions, performed a disservice in appending the designation of syncytioma or atypical chorionepithelioma to the lesions of the sort described in the present paper. To my mind, they do not represent tumors at all. Trophoblastic infiltration of both the decidua and the uterine musculature is observed in normal pregnancy, though to different degrees at different phases and in different women. However, it is often rather massive, and has in innumerable cases led to the wrong diagnosis of chorionepithelioma. It is a rather common residual finding when the uterus has been removed following the evacuation of a hydatidiform mole, and here again the frequency of incorrect diagnoses has vitiated statistics as to the incidence of genuine chorionepithelioma.

This is not the place for any dissertation on the frequently difficult problems of histological differentiation involved. However, one point to be stressed is that the benign or even normal trophoblastic infiltration is one of individual cells, actually believed by many embryologists to possess ameboid activity, while with genuine chorionepithelioma the trophoblastic tissue, not infrequently possessing so-called anaplastic characteristics, invades in large cell masses of usually both types of trophoblast, destroying the uterine musculature as it advances, as shown by the hemorrhage and necrosis noted histologically. This is only one tiny facet of a big question, but it is obvious that I agree with the authors that syncytial endometritis or deciduitis is a better term than syncytioma for the lesion which they describe in their report.—Ed.

varying periods of time positive 'takes' were obtained in about 60 per cent of the animals. Such lesions were nodular and cystic. Microscopically, these nodules were made up of islands of endometrium, some of which had the typical appearance of miniature uterine cavities. Some of them also showed proliferation of smooth muscle fibers and embryonal cytogenic stroma. These experiments demonstrate the comparative ease with which experimentally implanted bits of endometrium can be made to grow in the rabbit, thus lending support to Sampson's implantation theory of endometriosis."

(The fact that endometrium can be experimentally transplanted to various other tissues has been amply demonstrated by various investigators in past years. The incentive for such studies was the epoch-making work of Sampson, first published in 1921, and, as a matter of fact, probably the first work on the experimental transplantation of endometrium was done by Sampson's colleague, Jacobson, who was able to grow endometrium on the peritoneum. While the purpose of this study was to substantiate Sampson's theory of the origin of endometriosis from endometrial tissue regurgitated into the peritoneum from the uterine cavity, it could not be accepted as evidence on this point, nor did Sampson himself so consider it. This work simply showed the transplantability of endometrium to other tissues, but did not of course establish that the aberrant endometrium of pelvic endometriosis reached the peritoneum from the uterus by way of the tubes.

Ravid's observations confirm the results of earlier investigators, such as Cheval (Cheval, M., Proc. Roy. Soc. Med. 27: 1395-1406, Aug. 1934), who as far back as 1934 published similar studies to show how readily endometrial tissues grow when transplanted into various structures. However suggestive such studies may be, they do not prove the correctness of Sampson's theory. The pros and cons of this have been discussed for many years. Sampson himself in his latter years felt that the etiology of endometriosis is not always the same, that it is often the result of transtubal transportation of uterine mucosa, but that in other cases it is the result of metaplastic changes in the peritoneum, or, in the case of the stumps of amputated tubes, metaplastic changes in the tubal mucosa. As a matter of fact, it was this last topic which he presented in his last paper before the American Gynecological Society, and in the discussion which followed a similar compromise concept was expressed by other speakers.—Ed.)

SYNCYTIOMA—SYNCYTIAL ENDOMETRITIS

R. A. REIS AND E. J. DeCOSTA

Michael Reese Hospital, Chicago, Ill.

Am. J. Obst. & Gynec., 56: 584-586, 1948

The diagnosis of syncytioma, or syncytial endometritis, is usually made after hysterectomy. Metastases, other than local in the vagina, have not been reported for this type of tumor. Patients who have refused hysterectomy, after diagnosis has been made by curettage, are known to have remained well. It seems probable, therefore, that this malignant-appearing tumor is benign.

The case is reported of a 50-year-old woman whose youngest child was 9 and who had menstruated regularly until 2 months before admission. During these

THE USE OF VAGINAL SMEARS IN THE DIAGNOSIS OF GENITAL CANCER

J. R. KERNODLE, W. K. CUYLER AND W. L. THOMAS

Duke University School of Medicine and Hospital, Durham, North Carolina

North Carolina M. J., 9: 11-17, 1948

The technique for obtaining and staining vaginal smears is described and the interpretation of smears is discussed.

Four cases are cited which illustrate the fact that the diagnosis of preinvasive cervical carcinoma can be made much earlier by the vaginal smear method than by biopsy.

Approximately 4750 smears from 1139 patients have been studied at Duke. Ninety-seven cases of genital malignancy were diagnosed by smears out of a group of 106 diagnosed by pathologic examination of tissue, an error of 9.1 per cent. False positive diagnoses were made in 28 of 1033 patients, a percentage of 2.7.

The important feature of this procedure is its potentialities as a screening method for the detection of early cancer and of the precancerous benign lesion. It is thought that the method will come to be a routine part of the complete physical examination of women. 3 figures.

(See comment on following abstract of paper by L'Esperance.—Ed.)

THE STRANG CANCER PREVENTION CLINICS

ELISE S. L'ESPERANCE

A Symposium

Dorothy Ekstrom	R. S. Sherman
Frances H. Bogatko	M. Deddish
Genevieve M. Bader	J. Scapier
J. H. Ewing	Isabel M. Scharnagel
Harriet C. McIntosh	Sophie Spitz
Isabel Knowlton	

Am. M. Women's Ass., 3: 131-146, 1948

This survey is an attempt to review the activities which have developed gradually in the Strang Cancer Prevention Clinics and to emphasize their intrinsic value in the early diagnosis of cancer. Detailed reports are given of the various clinical research problems sponsored by these Clinics and the merits of each project are analyzed with a description of the method used.

UTERINE BLEEDING

E. HENDRIKSEN

Los Angeles, Calif.

Ann. West. M. & S., 2: 223-224, 1948

The author warns against the often hastily assumed diagnosis of functional uterine bleeding and the indiscriminate use of hormonal therapy. The most valuable diagnostic adjuvant in uterine bleeding is the curette, as it not only will often make the diagnosis, but quite frequently brings about an apparent cure. Only after cancer has been excluded should another diagnosis be considered. A pathological interpretation of endometrial hyperplasia must be carefully differentiated from endometrial polyps, irregular shedding, irregular ripening and retained secundines.

Fundal carcinoma may occur in the earlier age groups and menstrual irregularities should not be brushed lightly aside. The presence of uterine fibroids does not always indict them as a cause of bleeding, and careful diagnostic study is necessary before advising hysterectomy. Careful diagnosis is essential to success in treating uterine bleeding.

(A short but sound discussion of the subject. Especially to be underscored is the author's warning against the "often hastily assumed diagnosis of functional uterine bleeding and the indiscriminate use of hormonal therapy."—Ed.)

THE EARLY DIAGNOSIS OF UTERINE MALIGNANCY

T. L. LEE AND H. F. FULLER

Kinston, North Carolina

North Carolina M. J., 9: 9-11, 1948

Since trauma and irritation are the most important factors in the production of malignancy, many uterine cancers could be prevented by periodic pelvic examinations and adequate postpartum care, with correction of any abnormalities present.

All cases of irregular vaginal bleeding must be considered as due to a malignancy until they are proved otherwise.

A careful history and physical examination, together with a biopsy, are essential for the early diagnosis of uterine malignancy.

The Papanicolaou method is a valuable addition to our armamentarium for the early diagnosis of uterine cancer.

(See comment on paper by L'Esperance below.—Ed.)

THE PRESENT INCIDENCE AND SURVIVAL PICTURE IN CANCER AMONG FEMALES IN CONNECTICUT

1935-1946

ELEANOR J. MACDONALD

Connecticut State Department of Health

J. Am. Med. Women's Ass., 3: 152-162, 1948

The author reports the following data on genital tract and breast cancer in Connecticut females from 1935 to 1946:

	DISTRIBUTION		MICROSCOPICALLY PROVED PER CENT	1935-1941 SURVIVAL RATE PER 100,000	1935-1946 SURVIVAL RATE PER 100,000
	Cases	Per Cent			
Corpus of Uterus.....	1577	7.7	88.8	26.4	83.1
Cervix of Uterus.....	2267	11.1	94.0	35.0	101.2
Ovaries.....	1173	5.7	91.0	11.3	34.5
Fallopian Tubes.....	16	.07	93.8	.1	.4
Vagina.....	87	.4	88.5	1.0	3.0
Labia Minora and Clitoris.....	35	.2	91.4	.3	1.5
Breast.....	5148	25.1	89.4	59.5	239.6
Nipple.....	31	.2	90.3	1.1	2.0

The percentage distribution of cancer in these sites by age is shown in the following table:

	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80+	UN- KNOWN	AVER- AGE
Corpus of Uterus.....	.2	2.1	4.8	18.1	32.1	28.7	11.4	1.9	.7	57.3
Cervix of Uterus.....	.1	2.3	14.1	29.7	29.1	17.0	6.2	.7	.8	51.5
Ovaries.....	1.6	4.8	10.3	24.3	30.5	20.5	6.3	1.1	.6	52.1
Fallopian Tubes.....	—	—	—	13.3	66.7	13.3	6.7	—	—	56.3
Vagina.....	1.3	1.3	5.2	20.7	22.1	22.1	18.2	9.1	—	59.5
Labia Minora and Clitoris.....	—	—	3.1	6.3	12.5	40.6	31.2	6.3	—	65.9
Breast.....	.1	1.6	9.0	24.7	24.6	24.1	11.9	2.7	1.3	55.8
Nipple.....	—	—	—	25.0	28.6	28.6	17.8	—	—	58.9

(In these 2 tables from Connecticut, one of the most progressive states in the country in the campaign against cancer, one is especially struck with the fact that the incidence of cervical cancer is apparently only about $1\frac{1}{2}$ times as great (7.7 to 11.1) as that of corporeal carcinoma, a proportion far smaller than that usually noted. The survival rates as reported for the 2 periods of 1935-41 and 1935-48 appear on the surface to note a tremendous improvement in the latter, but it is impossible to make any intelligent comment on this point without knowing something about the basis for these figures. Certainly they appear out of line with the improvement noted generally throughout the country.—Ed.)

A statistical report for 1946 is presented for the Kate Depew Strang Prevention Clinic, Women's Division. During this year, 3,925 new female patients were examined. Of these, 361 failed to return for special examinations and have therefore been deducted from the total group. In the remaining 3,564 patients, 37 cases of cancer were found, or 1.03 per cent. The cancers were found in the cervix uteri (11), rectum, breast (10), fundus uteri (3), skin, stomach and kidney. In addition, precancerous lesions were found in 526 or 14.8 per cent of the total group. Approximately 5,000 former patients returned to the clinic in 1946 none having been seen less than one year previously. In this group 6 cancers were found, or .12 per cent.

During 1946, 4,160 females had vaginal and cervical smears as a screening method for the detection of early carcinoma of the generative tract. Of the number examined, the smears of 14 patients were diagnosed "positive" or "highly suspicious" for carcinoma. In 13 of the cases, biopsies confirmed the findings of the smears. One case has yet to be confirmed by biopsy. This screening method for cancer revealed one case of carcinoma of the female generative organs per about 350 patients. The technique for obtaining smears is described and a classification of reports of smears as applied to the diagnosis of genital malignancies is presented with accompanying photomicrographs. 5 figures.

(It appears fitting that medical women should have played such a prominent pioneer part in cancer detection work among their own sex, and the author of this paper, together with Dr. Catherine Macfarlane of Philadelphia, has played a conspicuous role in this respect. It is of interest that in the Strang Clinic, as in most cancer detection clinics, the use of the vaginal smear has become routine, but that it is employed only as a screening method rather than as a decisive method of diagnosis. This is in conformity with the opinion of all sound workers in this field, in spite of the statement made by Kernodle, Cuyler, and Thomas that the "diagnosis of preinvasive cervical carcinoma can be made much earlier by the vaginal smear method than by biopsy.")

I rather think that these authors must mean that such a diagnosis can be suspected from vaginal smears, as I do not see how anyone can distinguish the individual cells of a preinvasive lesion from those of an invasive one, for they are exactly alike. Furthermore, without supplementary biopsy of one sort or another, I do not see how anyone can speak of a lesion as preinvasive or invasive. For that matter, even a simple biopsy can not always make this distinction, so that repeated biopsies may be necessary. Kernodle and his co-workers, however, are right in emphasizing the potentialities of the vaginal smear as a screening method, although they may seem a bit utopian in thinking that it will come to be a routine part of the complete examination of women.

The short paper of Lee and Fuller adds nothing new to the subject. Many will question the statement that "trauma and irritation are the most important factors in the production of malignancy," although every one agrees that irritation of the chronic type may play a definite predisposing role, and that the correction of such irritative conditions is an important part of cancer prophylaxis. More important, however, is that unknown genotypic factor, in which heredity probably plays at least some part, and which unfortunately is often so strong that a group of body cells undergoes that somatic mutation which converts them into the killer cells of cancer, in the entire absence of any irritative lesion of any sort.—Ed.)

a spotless record which not many institutions can match, although in many hospitals radiotherapy was the uniform method of treatment until very recent years. As a matter of fact, there are only a few departures from it even today in many clinics. As yet those who stress surgery in a selected group have not made out a convincing case, but there has been an increasing resort to surgery, of either very radical or more restricted type, in the treatment of this small group. The evaluation of cancer treatments is a matter of years, and there is still a deplorable lack of anything like standardization of technics and evaluation of clinical stages among those who report results. A good many years will therefore elapse before the present day differences of opinion can be reconciled, and in the meantime it is quite certain that other worrisome issues will have arisen.—Ed.)

CANCER OF THE FEMALE GENERATIVE ORGANS

A. N. ARNESON

St. Louis, Mo.

Kentucky M. J., 46: 146-151, 1948

Particular advances in the treatment of cervical cancer may not show immediate improvement in survival rates but may aid in obtaining better regression of the tumor with lesser amounts of damage to normal tissue and fewer sequelae of treatment. This, the author feels, is particularly true of the use of radium.

It is suggested that the gynecologist engaged in treating cancer needs to perform a bimanual examination with a single intravaginal finger in order to avoid trauma resulting in ulceration and bleeding. Palpation of all vaginal fornices is an important step in diagnosis.

The three gross types of carcinoma of the cervix, the everted, infiltrating and cratered forms, are reviewed. Attention is called to the greater radiosensitivity of the everted and cratered types. Infection affects adversely the response to radiation by lowering the threshold to necrosis. Then destruction of the normal tissues of the tumor bed can result in unrestrained growth of cancer due to the removal of the normal inhibitory mechanisms.

The importance of continuing the examination in search of extension of the disease after the recognition of the primary lesion is stressed. The League of Nations classifications are pictured as blocks of tissue, each of different volume and with roughly defined boundaries. Biopsy is recommended as the fundamental basis of all diagnosis.

The author believes that the trend towards the use of greater amounts of x-ray as a first step in treatment is unwise as it delays the use of radium therapy and causes stenosis of the cervical canal. Intravaginal x-ray can supplement that given to the pelvic fields, but it is necessary to inspect the cervix frequently and to be assured of the canal's patency.

In planning radium treatment the nature and character of the individual lesion,

GYNECOLOGIC ASPECT OF CANCER

W. E. COSTOLOW

Los Angeles Tumor Institute, Los Angeles, California

Ann. West. Med. & Surg., 2: 120-121, 1948

Irregular bleeding around the menopause should always be considered a serious symptom, and careful examination may bring to light an early cervical cancer. A large, lacerated, eroded cystic cervix should be regarded with suspicion and should be biopsied. A scalpel or biopsy punch is the method of choice. A large biopsy which might require stitches and cauterization following the procedure is to be avoided. These may cause sloughing and infection and subsequent radium treatment may produce a pelvic cellulitis.

Only about 10 per cent of cervical cancers are detected in the early stages. The early symptoms are often vague and unreliable. Prolongation of periods, bleeding between periods or bleeding after intercourse are alarm signals. At the Los Angeles County General Hospital, no primary cases of carcinoma of the cervix have been treated surgically during the past 10 years. Instead, all cases are referred for irradiation regardless of the stage of the disease.

Probably 50 per cent of women with bleeding a year or more after the menopause have cancer of the uterus and 75 per cent of adenocarcinomas of the fundus develop after the menopause. In the author's clinic it is the policy not to use any type of endocrine therapy for alleviation of menopausal symptoms in patients with cancer who have been treated by radium and roentgen therapy. In over 2000 patients with uterine cancer, severe menopausal symptoms have occurred only rarely. Treatment of the uterine cancer is surgery supplemented by pre- and post-operative radiation therapy.

Care of the patient with advanced cancer of the pelvic organs deserves the same attention as any other chronic disease. Modified radiation therapy should be used when practical. If the cure rate is to be increased in this group of patients, earlier diagnosis and treatment must be instituted.

(The author's statement that only about 10 per cent of cervical cancers are detected in early stages presumably means that that figure represents the incidence of Stage 1 cases in his clinic. But the figure would be far too high if it referred to the very early cases, including even those of preinvasive type, which are now receiving such intensive study. The majority of the Stage 1 cases present a definitely suspicious lesion and in such cases biopsy, often multiple, will usually detect cancer if it is present. However, there are exceptions and in these cases thorough scraping or paring of the squamous margin throughout its entire circumference will sometimes reveal the lesion which the ordinary biopsy may miss. This is the so-called surface biopsy which I have plugged so often that I am almost ashamed to mention it again, although I personally believe that it affords a far more comprehensive and more frequently decisive picture of the status of the cervical squamous epithelium than can be obtained either by vaginal smear or by even multiple biopsies of the ordinary type.

It is of interest to note that not a single case of cancer of the cervix has been treated surgically at the Los Angeles County General Hospital during the past 10 years. It is

accurately expresses my own attitude on this much discussed subject. The authors call attention to the fact, as I have repeatedly done in these pages, that a large proportion of the positive smears reported in cervical cancers is made up of cases in which the diagnosis is either obvious or easily made by biopsy. Certainly a smear is not necessary in cases of Stage 4 or 3 or 2, or in all but a minority of Stage 1 cases, those in which the lesion is very small or totally invisible. The real test would of course be in women whose cervixes appear entirely normal and in which even multiple biopsies of the ordinary type might still miss the lesion. In these cases the smear can concededly play a valuable screening role to be followed by more intensive and more decisive biopsy study. Even with no such thing as vaginal smears, one might, as the authors state, "submit a brief to the effect that practically every case of carcinoma of the cervix could be detected at a stage when the disease actually did not constitute a threat of life." On the basis of what appear to be valid statistics and estimates, the authors figure that "it would require 500 hours of microscopy to detect 1 carcinoma of the cervix from the general population of women 35 years of age or over." Again, "promotion of the use of the smear method is apt to originate from persons who are not doing the actual work." The authors, indeed, suggest the advisability of transferring the burden of smear method diagnosis to a talented technical personnel, although at present it seems almost utopian to hope that in the foreseeable future there will be anything like an adequate number of available technicians of this sort.

This whole short paper happens to be "right down my alley," and hence I recommend its reading to all those interested in vaginal cytological studies, especially the not inconsiderable group of over-enthusiasts.—Ed.)

THE USE OF THE VAGINAL SMEAR IN THE DIAGNOSIS OF CANCER

H. ULFELDER

Boston, Mass.

Connecticut M. J., 12: 513-514, 1948

Almost 20 years have elapsed since Papanicolaou first described his technique of cytological examination, and since that time there has been widespread acceptance of this diagnostic procedure. Many modifications of the original procedure have been advocated; however, the simplicity of the original method lends itself readily to the office practice of any physician. The characteristics of abnormal cells are hyperchromatism of their nuclei, wide variations in nuclear size, loss of normal nuclear-cytoplasmic ratio, and disappearance of cellular borders when they occur in groups.

In the series studied by the author, the first smear was reported positive in 1.6 per cent of 3258 cases without malignant disease, and 12.9 per cent of the first smears were reported negative in 372 cases with malignant disease. The incidence of error was higher in endometrial lesions, with the smear reported negative in 10.1 per cent of cervical cancers and in 20.6 per cent of endometrial cancers. In several cases of false positive smears, serial section has revealed exceedingly small cancers which were invisible to the naked eye.

It is not supposed that this method of diagnosis can ever replace biopsy, but

the degree of infection and the amount of biologic change the tissues will tolerate must be considered. The sources of radium at hand should be studied and a rough diagram of each arrangement of the tubes will be helpful in the planning. It is of great benefit to think in terms of doses per tube rather than in terms of total milligram hours. Several examples of the possible arrangement of tubes of varying lengths and intensity to produce the same biologic effect are given. The author believes that whenever the total amount of radium exceeds 100 mgs. it is seldom practical to exceed more than 5,000 mg. hrs. at a single exposure. For smaller amounts of radium, 6,000 to 8,000 mg. hrs. may be given. The author concludes that there is great possibility for advancement in treatment by increasing the knowledge of radiation and of the physical principles of irradiation.

(This paper, by one who has contributed greatly to the development of the technical details of radiation therapy for uterine cancer, and whose skill in this field has been reflected in the results which he has reported, is devoted largely to the general principles of radiation therapy. Anyone interested in the subject will find the paper well worthwhile.—Ed.)

SMEAR DIAGNOSIS OF IN SITU CARCINOMA OF THE CERVIX

F. W. FOOTE AND KATHERINE LI

*New York State Department of Health and Memorial Hospital,
New York, N. Y.*

Am. J. Obst. & Gynec., 56: 335-339, 1948

The authors postulated that in many reports carcinoma of the cervix found by the smear method would have been easily detected by other diagnostic procedures. However, in in situ or noninvasive carcinoma very little has reached the literature concerning smear diagnosis, and such tumors constitute the real test of the value of the method. Eighteen cases of in situ carcinoma are reported and in none of the cases studied by repeated sections was infiltration discovered. In 14 cases the smear taken directly from the cervix gave unequivocal cytologic evidence of the presence of carcinoma, and in 9 cases the smear of the vaginal vault was positive. All of the cases were asymptomatic and, hence, a large proportion would have been overlooked without the smear diagnosis.

The authors also discuss the advisability of doing cervical or vaginal smears on all women over 35 years of age. They point out that studies of incidence indicate that theoretically it would require 500 hours at the microscope to discover one case. The only reasonable solution would seem to be the transference of the time-consuming job from the pathologist to highly trained technicians. The fate of smear diagnosis rests on the skills developed in its interpretation.

(This paper is to my mind one of the most sensible and cogent comments on the subject of the vaginal smear diagnosis of cervical cancer which I have seen, probably because it so

the usual hyperchromatic character of atypical cells, combine to make this a useful stain in the diagnosis of uterine cancer by the vaginal smear method.

The cytoplasmic and nuclear characteristics of cells impregnated with silver carbonate are described and several advantages of the technique over other conventional differential stains are listed. 9 figures.

(See comment on abstract of paper by Cromer, Platt and Winship, below.—Ed.)

UTERINE CANCER: ITS EARLY DETECTION BY SIMPLE SCREENING METHODS

D. J. MCSWEENEY AND D. G. MCKAY

Boston City Hospital, Boston, Mass.

New England J. Med., 238: 867-870, 1948

A report is made on the operation and success of a cancer detection clinic established a year ago in the Boston City Hospital. All other departments in the hospital referred women over 35 years for the screening process. Screening consisted of gynecological history with attention to abnormal bleeding and vaginal discharge, a pelvic and a speculum examination, and a vaginal smear. The smear was used to indicate the necessity for a curettage or biopsy. Treatment was never instituted on the basis of the smear alone. A positive smear and a negative biopsy called for monthly inspections of the patient and repeated smears and biopsies. All obviously negative cases were re-examined every six months.

One of the major interests of the study was to determine whether or not unsuspected cases of carcinoma could actually be detected by the vaginal smear method. Technique and cytology of the smear method are briefly discussed.

Results of the study of 639 cases are presented. Fifty-four cases of carcinoma were determined by biopsy. In 51 of these the vaginal smear was positive, an accuracy of 95%. Two of the patients with false negatives had vesicovaginal fistulas and the other had uterine bleeding.

A correct negative smear was found in all but 12 of the 585 patients demonstrated not to have cancer. This false positive group was 2% of the cases diagnosed negative by smear and 4% of those diagnosed by biopsy. No treatment was instituted without a positive biopsy.

Six cases were diagnosed primarily by smear. One patient with positive smear and negative biopsy returned ten months later and again had a positive smear. A biopsy done at this time was diagnosed carcinoma in situ. Abstracts of 12 typical cases are presented.

The authors feel that this method of screening is efficient and effective in the early diagnosis of cancer. The degree of accuracy depends upon the care with

in combination with biopsy cancer of the cervix has been demonstrated in 98 per cent of cases. The method is also useful for singling out patients for further investigation.

(See comment on abstract of paper by Cromer, Platt and Winship, below.—Ed.)

VAGINAL CYTOLOGIC SURVEY IN GYNECOLOGIC CANCER

V. PARRETT, C. SMALL AND L. WINN

White Memorial Hospital, Los Angeles, Calif.

Am. J. Obst. & Gynec., 56: 360-365, 1948

The authors had noticed that a large number of genital cancers were being found only after they were far advanced. Because of this, routine vaginal smears were done on all new admissions to the gynecology clinic, primarily to see if cancers might in this way be discovered which would otherwise be undetected.

Of the first 1000 consecutive gynecologic patients, 958 had negative smears. Of these, 4 had previously received radiation for known uterine cancer. In 42 cases the smears were positive or suspicious. Of these 42 cases, 25 had carcinoma as proved by biopsy. Seventeen had no carcinoma but were proved on biopsy to have papilloma of the cervix, functional bleeding, cervicitis, leukoplakia or uterine myoma. The authors concluded that the vaginal smear was a reasonably accurate cancer exclusion method but a less accurate diagnostic method. It may often be a method of cancer detection leading to diagnosis in certain cases where clinical evidence is lacking.

(See comment on abstract of paper by Cromer, Platt and Winship, below.—Ed.)

THE APPLICATION OF A SILVER CARBONATE STAIN FOR THE DIAGNOSIS OF UTERINE CANCER BY VAGINAL SMEAR METHOD

H. S. YUE, G. M. RILEY, N. F. MILLER AND K. SCHARENBERG

University of Michigan Hospital, Ann Arbor, Mich.

Am. J. Obst. & Gynec., 56: 468-476, 1948

The silver carbonate staining method of Hortega was modified for staining the cellular elements of vaginal smears. The writers describe the details of the procedure. The affinity of chromatin material for the silver stain, together with

cancer is shown by illustrative reports. The value and limitations of the method are set forth.

(The spate of papers on vaginal smear diagnosis still continues, but it is evident that opinion has pretty well crystallized to the effect that its chief value is as a screening method, that it has a definite supplementary value to biopsy, but that it is on the latter that we still have to depend for the decisive diagnosis which will point the way to treatment. The pitfalls of vaginal smear diagnosis are illustrated by the report of Cromer, Platt and Winship that in 30 patients with known cancer proved by biopsy fully 11 (28.95 per cent) were reported as negative for cancer. I do not mean to be supercilious in stressing the limitations of vaginal smear diagnosis, which are fully appreciated by the real experts in the field, but I would hate to see gynecologists lose sight of the woods for the trees by neglecting biopsy in an injudicious scramble for the vaginal smear bandwagon, to use a very weird metaphor.—Ed.)

A COMPARISON OF THE ACCURACY IN DIAGNOSIS OF THE VAGINAL SMEAR AND THE BIOPSY IN CARCINOMA OF THE CERVIX

RUTH M. GRAHAM, S. H. STURGIS, AND J. MCGRAW

*Vincent Memorial Hospital, Massachusetts General Hospital,
Boston, Mass.*

Am. J. Obst. & Gynec., 55: 303-307, 1948

It is the intention of the authors to examine the cytologic and histologic methods of diagnosis in carcinoma by a comparison of the initial vaginal smear and cervical biopsy in proven cases of cancer of the cervix.

The cases were limited to those with primary epidermoid cancer. Only cases where smear and biopsy were done before radiation, and where both specimens were available were used. One hundred eighty-one cases were included that had been examined at the Vincent Memorial Hospital laboratory.

In 148 or 82% both the first smear and the biopsy were positive for carcinoma. There were 19 cases or 10% in which the first biopsy was negative. There were 3 reasons for this failure: first, the failure of the surgeon to choose the right area for biopsy; second, errors due to misinterpretation of the specimen; and third, insufficient tissue for diagnosis.

There were 17 cases or 9.4% in which a negative vaginal smear was reported. On review 8 showed cancer cells. Three reasons for this failure were: one, occasionally the tumor did not desquamate cells into the vagina; two, cancer cells were not seen on the first examination, and three, the misinterpretation of cancerous cells as benign.

There was only a 1.7% error in the initial diagnosis of the combined results of both methods indicating that each method was complementary to the other.

which the smear is taken and the training and experience of the cytologist. 4 figures.

(See comment on abstract of paper by Cromer, Platt and Winship, immediately following.—Ed.)

THE COLPOCYTOLOGICAL (PAPANICOLAOU) METHOD OF DIAGNOSIS OF UTERINE CANCER

A PRELIMINARY REPORT

J. K. CROMER, LOIS I. PLATT AND T. WINSHIP

*Warwick Memorial Clinic, National Cancer Institute and Garfield
Memorial Hospital, Washington, D. C.*

M. Ann. District of Columbia, 17: 272-276, 1948

The authors present a preliminary report on the institution and use of the vaginal smear method of diagnosis of uterine cancer in a cancer prevention and a cancer treatment center. From January, 1947, to October, 1947, 295 smears were prepared from 290 patients at the Garfield Ladies' Aid Cancer Prevention Clinic. Of these, 287 smears (97.3 per cent) were reported negative for cancer, and 8 smears (2.7 per cent) were reported positive for cancer. Of the 7 patients on whom the 8 positive smears were recorded, one was proved to have adenocarcinoma of the fundus by diagnostic curettage. Two were found not to have cancer by subsequent biopsy. Of the remaining 4, who were returned to their physicians, biopsy was not considered necessary by those physicians in 2 cases, and there is no follow-up on the other 2.

Of the 290 patients in this series, 34 either had abnormal pelvic symptoms or findings; all smears in this group were reported negative. Of this group, 21 were returned to their physicians who failed to submit follow-up reports; 8 were treated by their physicians with biopsy; and 5 were proved non-cancerous by biopsy.

A second series of smears was made in the Warfield Memorial Clinic from November, 1946, to August, 1947. These patients had clinical carcinoma of the cervix and were proved by biopsy to have cancer. In this group 38 smears were made on 30 patients with 27 (71.05 per cent) reported positive for cancer and 11 (28.95 per cent) reported negative for cancer. This percentage of negative smears on patients with positive findings is entirely too large and not in keeping with recent reports. A combination of time, effort and experience will bring more accurate results.

The application of the vaginal smear method in the diagnosis of asymptomatic and unsuspected uterine cancer and in the selection of radio-resistant cervical

The daily dosage of roentgen irradiation has usually consisted of 180 r delivered to each of 2 portals. A combination of 2 to 6 portals has been utilized, so arranged and treated as to deliver a total dosage of about 2,500 to 3,000 r into the midpelvis. Radium has usually been delivered in a series of 2 to 4 intrauterine applications spaced about 10 to 14 days apart. Total dosage has varied from 4,000 to 8,600 mg. hours.

The authors discuss the motives behind this fractionation of radium and its combination with high voltage roentgen therapy. A carcinoma shrinks progressively during constant pounding with roentgen rays and even more rapidly after each concentrated blow with radium. This progressive shrinkage permits each successive radium application to approach more and more closely to the basal periphery of the neoplasm.

Since 1937, it has been advised that as many patients as possible be treated as follows: After the diagnosis has been established by a diagnostic curettage, the carcinoma is subjected to high voltage roentgen therapy and intracavity radiation, followed in about 8 to 12 weeks by surgical treatment, depending upon the general condition of the patient and the extent and operability of the lesion.

Since 1937, 35 patients have been submitted to high voltage roentgen therapy and intracavity radiation. From 1937 to 1941, 15 patients were treated with preliminary high voltage roentgen irradiation and radium. Only 3 were selected for surgery. Of the remaining 12 patients, 7 died from intercurrent disease or carcinoma within 2 years, and 5 lived for 5 years or more. Thus, a total of 8 patients survived, or 53.3 per cent.

From 1942 to 1946, 20 patients were treated by the method just described, and 6 were selected for surgical treatment; 3 more are to be operated on. Seven patients not operated on have died of intercurrent disease or carcinoma, and one patient operated on died one year later. This is a total of 12 patients surviving for one to 5 years, or 60 per cent.

In 9 of the 35 cases, therefore, carcinoma was considered operable and pan-hysterectomy was carried out. One patient has died since operation, the exact cause being unknown. One patient has survived for 9 years, 2 for 7 years, one for 6 years, one for 4 years, 3 for 3 years and one for 2 years.

Although the presented series of 9 cases is too small from which to draw conclusions, it is hoped that the results will stimulate others to investigate the possibilities of combined roentgen therapy and intracavity radiation followed by surgical intervention as a means of obtaining a higher salvage of patients affected with carcinoma of the fundus uteri.

(This paper abstracted above exhibits a commendable effort at individualization of treatment, but the authors' report of past experience is a rather unorthodox one at the present day. Only 3 of 35 patients from 1937 to 1941 were selected for surgery, and only 6 of 20 from 1920 to 1946, but the results in the small group of surgically treated patients would seem better than those treated only with radium and X-ray. Although the series is a small one, it appears to justify the present day popularity of including hysterectomy as an essential part of treatment, but of preceding it with radiotherapy. However, a number of discordant notes have been recently sounded in the literature questioning the advantages of preliminary radiation, and I for one, have made frequent exceptions in my own practice, as in the

One should not be used to the exclusion of the other, as they serve as checks upon one another.

By classifying preinvasive cancer as stage 0, it was noted which method was more reliable in diagnosing early lesions. Of the 17 cases of false negatives by vaginal smears only 8 were in stage 0. However a majority of the cases missed by biopsy, 15 out of 19, were early cases. There was a total of 16 cases of stage 0 cancer in the entire study. Therefore the author feels that the vaginal smear is of special value in the diagnosis of early malignant lesions of the cervix.

The author also concludes that the vaginal smear is diagnostically as reliable as the biopsy taken in a large general hospital and that an extremely high percentage of cases can be diagnosed accurately if the two methods are used together. 4 tables.

(The question of vaginal smears in the diagnosis of cervical cancer has been discussed in these pages on numerous occasions in the past. The present paper, by one of our leading vaginal cytologists, is of considerable interest, but I believe it may be misleading to some. In the hands of an expert I believe it quite likely that vaginal smears might reveal malignancy more frequently than biopsy if the latter is of the random type which it usually is in the absence of any suspicious lesion of the cervix. But if the biopsy is of the type of comprehensive surface scraping of the epithelium in the vicinity of the epithelial junction, it is difficult for me to believe that it would not yield more information than a smear and, what is more important, information which could be intelligently interpreted by any well-trained pathologist and not only by that *rara avis*, the really well-trained vaginal cytologist.

But the contrast above mentioned applies only to the screening process in women with no clinical suspicion of the disease, and certainly in this field the employment of vaginal cytology should be encouraged, with due regard for its supplementary value to the more decisive value of subsequent biopsy study.

On the other hand, when a definitely suspicious lesion of the cervix is revealed by careful inspection, I for one would do a biopsy rather than a vaginal smear, and with very little fear that, with careful histologic study, a cancer would be missed if it is present in the lesion. This point seems to me well worth emphasizing, for I have gotten the impression that some gynecologists are missing the trees in looking for the woods, and that the tried and true 75 year old method of biopsy is sometimes neglected in the enthusiasm for the new fangled method of vaginal smears. If this makes me a reactionary, I am afraid that I shall have to plead guilty.—Ed.)

TREATMENT OF CARCINOMA OF THE FUNDUS UTERI

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Arch. Surg., 56: 172-177, 1948

The program of treatment of cancer of the uterine body with radium and high voltage roentgen irradiation at the University of Nebraska Hospital is characterized by individualization in each case, fractionation of the radium and correlation of high voltage roentgen irradiation and radium therapy.

forth. Some believe that the drying effect of the air is the protective influence, the factor of cornification being a corollary of such a theory. If the question could be clearly solved, we might conceivably learn a good deal about the prophylaxis of cervical cancer.

I recall only 2 personal cases of this sort. In the first of these, observed a good many years ago, a radical vaginal hysterectomy was performed by the Schauta technic, and the patient remained free of cancer for 8 years, when she died of cardiovascular disease. In the second case, somewhat more advanced, radiotherapy was used, but the patient died approximately 3 years later.—Ed.)

ATYPICAL ENDOMETRIAL HYPERPLASIA SIMULATING ADENOCARCINOMA

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Am. J. Obst. & Gynec., 55: 46-61, 1948

The purpose of this paper is to call attention to a group of benign hyperplastic lesions of the endometrium which may be and often have been mistaken for adenocarcinoma. While these lesions are actually hyperplastic in a general pathological sense, they are very different in their histologic characteristics from the ordinary type of benign Swiss-cheese endometrial hyperplasia.

The histologic appearance of any part of the endometrium is determined not only by the hormonal influence to which it is subjected, but also by its own degree of sensitivity or refractoriness to the hormones in question. The degree of maturity or immaturity, ripeness or unripeness of the endometrium, appears to be the most important factor in determining the degree of its receptivity to the ovarian hormones. In general it seems to be true that young, immature endometrium is highly responsive to the growth effect of estrogen and refractory to the differentiating hormone, progesterone.

The histologic picture presented by the ordinary Swiss-cheese hyperplasia does not in the slightest degree resemble that of adenocarcinoma. The ordinary hyperplasia observed during reproductive life has no tendency toward malignant transformation.

The writers have been impressed with the fact that the simple type of Swiss-cheese hyperplasia does not represent the only abnormal endometrial pattern which may be produced by excessive or prolonged estrogen stimulation, either in the human female or in the experimental animal, and that these other growth patterns are often totally different in histological appearance from the Swiss-cheese type.

A good illustration of the variations in the histologic effect produced by the same estrogenic agent is seen in the examination of the endometria of women who have been taking diethylstilbestrol, often in considerable dosage, continuously for inordinate lengths of time. No gynecologist need be told that the

case of early lesions. It does not seem to me that such advantages of preliminary radiation as sterilization of the cancer area and the entrapment of cancer cells are of great importance in early cases, while the possible hazard of disseminating cancer cells is avoided by such simple precautions as suturing the cervical canal and the early application of broad ligament clamps at the hysterectomy.—Ed.)

CARCINOMA OF THE CERVIX COMPLICATING PROCIDENTIA UTERI

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Am. J. Obst. & Gynec., 55: 299-302, 1948

Two cases of carcinoma of the prolapsed cervix are presented. The first was a 74 year old woman admitted to the Woman's Medical College Hospital of Pennsylvania. There had been some protrusion for about 4 years and the uterus had been prolapsed at all times and was replaceable. On physical examination a uterus the size of a small orange was found protruding from the vaginal opening and on the lower portion there was a fungating, bleeding, irregular mass twice the size of the uterus. A biopsy of the cervix revealed an infiltrating malignant tumor arising from stratified squamous epithelium. The impression was grade 3 carcinoma of the cervix.

Treatment by x-ray, radium and operation were proposed in this order. Approximately 4,000 R. U. were given to the tumor. But the patient developed large ulcerations on each thigh and was discharged to return later for radium. In 4 weeks the uterus was small enough to be replaced and a Menge pessary was inserted in order to improve the physical and mental condition of the patient. Cystoscopic examination showed a deep sloughing area in the posterior lip of the cervix. Therefore radium was abandoned. The patient died after 6 weeks.

The second case was aged 47 years, gravida 8. She had had some prolapse for 13 years and procidentia for 2 years. The biopsy was diagnosed as squamous cell carcinoma. 4,800 mg. hours of radium were used and later a vaginal hysterectomy was done. There was some recurrence 7 years later but she still survives.

The incidence of cancer with procidentia is strikingly rare. The chief theory used to explain this is that cornification of the epithelium raises the resistance to cancer. Emmert and Taussig challenge this with reference to the frequency of carcinoma in the lower lip of the face. The question remains unsettled.

In treatment x-ray should be used first as it gives a uniform radiation, combats infection and shrinks the tumor. Radium can then be used after the uterus is replaced.

(The rarity of cervical carcinoma in association with complete prolapse has always provoked interest, but, as the author remarks, no satisfactory explanation has been brought

obvious epithelial dedifferentiation, nuclear changes or even invasiveness, which make the distinction easy. But other common microscopic characteristics of adenocarcinoma are no less marked, and sometimes more so, in certain of these atypical hyperplastic processes than in the actually malignant one. It is another way of reiterating what most pathologists have always emphasized, that a lesion either is or is not cancer, but that in individual cases it is simply impossible to make the decision by microscopic examination.

After all, the decision as to whether or not a given lesion is malignant or benign could best be made by the patient herself, were we to let her unfold her own story to recovery or ultimate death. But we cannot use the human patient as a laboratory experimental animal. We must therefore do our best to separate these atypical lesions into two groups: (1) one in which, in spite of certain atypical characteristics, we can be quite certain that cure can be effected by simple conservative treatment, thus avoiding extensive surgery, which is not without hazard, and which also imposes on the patient the cloud of future uncertainty which is the inevitable lot of every cancer patient; (2) the group in which the possibility of already existing cancer cannot be eliminated, and in which conservative treatment might dangerously delay adequate cancer therapy.

The authors are convinced that every case in their Group I was nonmalignant, and they would not hesitate to employ conservative methods in the type of endometrial lesions found in this group. They are unorthodox enough to feel that all or nearly all of the lesions described in their Group II patients were also not malignant, and yet they are convinced that such pictures are very often interpreted as adenocarcinoma. As a matter of fact there are few who would have the courage to withhold radical treatment in such cases. In these genuinely uncertain cases the writers themselves practice this plan, although the time will probably come when we shall have available some more precise means of sifting out the benign lesions from those in which the irrevocable cancer mutation has occurred.

The fact that 44 instances of these questionable lesions have been revealed by a survey of the authors' material which is not by any means exhaustive, leads them to believe that in the aggregate they are numerous enough to have some vitiating influence on cancer statistics. Mistakes in pathologic diagnosis are of course inevitable in all fields of pathology, but the writers believe that in the endometrium, as in the breast, such misinterpretations are disproportionately common because these organs are under the physiological influence of estrogen. The ability of estrogen to produce pseudoneoplastic lesions in both the uterus and the breast has been abundantly established by experimental studies, and it is believed that the lesions described in this paper belong in this category. 16 figures.

abuse of this drug, in itself a very valuable one, is a widespread evil, and that postmenopausal bleeding is a frequent result of such injudicious therapy of menopausal vasomotor symptoms. The writers have had the opportunity of examining a number of endometria of such patients, and of noting that the hyperplastic effects of the drug vary greatly in degree and in character. While in some cases they are of mild degree and usually of benign Swiss-cheese character, in the occasional case they are very atypical, with such high degrees of adenomatous and proliferative activity that they may easily be mistaken for adenocarcinoma.

The authors list some of the atypical proliferative patterns which may lead to the incorrect diagnosis of carcinoma as follows: (1) increased number, crowding, and moderate atypicalness of the glands; (2) stratification, abnormal staining, and atypical morphology of the epithelium; and (3) the presence of squamous plaques in the walls of the glands, and occasionally on the surface. All these variations are illustrated in the 16 photomicrographs which accompany the paper.

The material forming the immediate basis for this study consists of a group of cases which show atypical hyperplastic changes which might readily be mistaken for adenocarcinoma, and which, as a matter of fact, were actually so diagnosed in many instances. These cases were selected from a considerably larger group exhibiting less pronounced atypical pictures which few would interpret as malignant. The question naturally arises as to the criteria on which the authors have decided that the lesions in question are not actually malignant. These are apparent from the grouping adopted for these cases with questionable histological characteristics.

In Group I, there were 18 cases receiving no treatment except curettage plus radiologic induction of the menopause. All remained well during the follow-up period. In Group II, there were 26 cases of atypical hyperplasia, with subsequent hysterectomy, without preliminary radiation. In none of these was any gross lesion found on examining the removed uterus, and all remained well during the follow-up period.

In the study of any very large number of hyperplastic endometria one will encounter every possible histologic gradation between the frankly benign and the obviously malignant. In the majority of cases of adenocarcinoma of the endometrium the malignancy arises in a normal, nonhyperplastic endometrium, and the contrast between the benign and the malignant area is usually clear enough. But the atypical hyperplastic endometria being discussed in this paper may present difficulties of diagnosis.

The fact that the histologic transition between the benign and the malignant lesions is marked by almost insensible transitions does not of course mean that these gradations indicate the gradual transformation of a benign to a malignant lesion. The important consideration is that the irreversible somatic mutation which transforms a normal epithelial cell into a cancer cell is probably of short duration, and in the beginning cannot as a rule be determined by any histological method now available.

Comparatively soon it may engender certain cruder characteristics, such as

which he mentions. Certainly no one would wish to attempt repair of a rectovaginal or vesicovaginal fistula produced directly by the cancer and surrounded by cancer tissue. On the other hand I have seen a number of instances of spontaneous closure of rectovaginal fistulas produced by the radiation attack upon the cancer, and this fact shows that the devitalization of tissues of which Maas speaks is not an insuperable bar to healing. I have also seen a number of instances in which such postradiation fistulas, either vesicovaginal or rectovaginal, were successfully treated by operation.—Ed.)

AN EVALUATION OF ADJUNCTIVE RADIOTHERAPY IN THE SURGICAL TREATMENT OF ENDOMETRIAL CARCINOMA

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Am. J. Obst. & Gynec., 56: 502-508, 1948

An analysis of 157 surgically treated cases of carcinoma of the endometrium at this hospital has shown no benefit from pre-operative irradiation with intra-uterine radium. The best results in the early cases and with tumors of low histologic grade were obtained by hysterectomy alone. A 5-year cure rate of 85 per cent was obtained by hysterectomy alone in early cases, and a cure rate of 91 per cent resulted from hysterectomy alone in histologic grade I cases. Post-operative x-ray therapy appeared to be of value in advanced cases and possibly for tumors of high histologic grading.

The writers feel that there is little theoretical basis for the intrauterine application of radium in patients who are to have subsequent hysterectomy for corpus cancer. If the tumor is limited to the uterus it is eradicable surgically. If it has already extended beyond the uterus it is beyond the reach of effective emanations from intracavitary radium.

(The prevailing trend—I came near saying fashion—in the treatment of adenocarcinoma of the endometrium is to give preliminary radiation, either by intracavitary radium or x-ray, with panhysterectomy approximately 6 to 8 weeks later. The as yet not too abundant statistical reports which are available appear to show better results than with surgery alone, but it cannot as yet be sure that this plan will endure. Already it is being challenged by some, though it takes a bit of courage to back the tide which has been set in motion by the well-known gynecologists urging the combined plan. I do not think there is any doubt that preliminary radiation does often destroy or devitalize cancer cells within the uterus, but there are many exceptions. Nor is there any doubt that radiation exerts a sterilizing effect upon the often necrotic cancer area, although in these days of antibiotics and chemotherapy peritonitis is not a greatly feared complication in operations in which the uterus is removed in toto. Again, it is quite probable that the fibrosis produced by radiation does cause a considerable degree of entrapment of cancer cells, and thus minimizes the risk of disseminating them by operative manipulation. But this latter risk, it seems to me, is practically eliminated by proper operative technic, such as preliminary closure of the cervical canal by suture and the early application of broad ligament clamps with also, if one so desires, ligation of the tubal extremities.

INTESTINAL CHANGES SECONDARY TO IRRADIATION OF PELVIC MALIGNANCIES

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Am. J. Obst. & Gynec., 56: 249-259, 1948

One of the most vexing problems in treatment of pelvic malignancies is the numerous pathological entities which arise subsequent to radiation therapy. The most distressing of the various possible lesions are the disorders of the rectum and sigmoid. Transitory and permanent pathological changes may occur, and to insure adequate radiation of the tumor, certain irreversible changes must ensue.

The author reviews 600 cases which received irradiation for pelvic malignancy, and of these, 523 suffered radiation sickness and 70 developed permanent rectal changes. The onset and course of radiation sickness was unpredictable but the most common symptoms were nausea, anorexia, lassitude, headache and nervous manifestations. Higher doses of radiation therapy tend to produce permanent rectal lesions earlier and of a more serious nature. Radium was a more serious offender than x-ray.

The bulk of permanent rectal changes following irradiation of the pelvis were due to factitial proctitis, and the rectosigmoid junction was the most frequently involved site. Specific symptoms usually developed in the order of diarrhea, bleeding, pain, constipation and finally fistula and obstruction. Management of these cases is grossly unsatisfactory and colostomy may be necessary if the bleeding becomes profuse or if obstruction is impending.

Other complications were less frequent but none the less serious. Rectal stenosis following radiation to pelvic malignancies occurred 48 times in this series. This process was irreversible. One case of rectal fibrosis without stricture was encountered. Rectovaginal fistula developed in 13 patients, in 2 of which spontaneous closure occurred. Radical treatment of such fistulae is never indicated and surgical repair is doomed to failure. Treatment is entirely symptomatic. Secondary carcinoma of the bowel occurred in 10 cases. One primary adenocarcinoma of the rectum developed in a case of squamous-cell carcinoma of the cervix.

(Any one who has ever had to deal with instances of postradiation "factitious proctitis" will appreciate that radiation therapy for cervical carcinoma is a two-edged sword and that in at least some cases the lot of the patient has been no less deplorable than that inflicted by the cancer itself. On the other hand, the now general recognition of such hazard has led to improvements in technic which have greatly lessened the incidence of serious visceral injuries, but certainly have not eliminated them altogether, as is obvious from the report of Maas. The radiation sickness which he encountered in such a large proportion is often highly disagreeable but not serious, but this cannot be said of some of the other sequelae

(Sarcoma of the uterus is relatively uncommon, occurring about $\frac{1}{40}$ times as often as carcinoma. Kardash's figure of 0.48 per cent as the incidence of sarcomatous degeneration in myomas is quite close to the figure of 0.56 per cent found in our laboratory in the study of 6,931 myomas (Novak and Anderson, *Am. J. Obst. & Gynec.* 34: 740, 1937). It is, however, lower than that reported by a number of other authors (Kimbrough 1.02 per cent, Kjaften 2.8 per cent). In any event, malignant changes in myomas do not occur often enough to justify the high-pressure emphasis put on this as a part of the "sales-talk" of some surgeons in persuading patients that operation is strongly indicated. Frequently, of course, it is, but more often on some other grounds. The hazard of late sarcoma in myomas is not comparable to the risk of either existing or subsequent malignancy in ovarian tumors. No matter how free of symptoms a patient may be, operation is always advisable when a definite neoplasm of the ovary is discovered, especially if the patient is middle-aged or old.

In almost all reports on sarcoma, as in the present one, a large proportion of the patients have had operations not as radical as they would have had if the nature of the tumor had been known at the time of operation. This is especially true of the cases which are secondary to myoma, and the surgeon is likely to get an unpleasant jolt when some days after doing a supravaginal hysterectomy or perhaps only a myomectomy, he gets a laboratory report of sarcoma. What to do in such cases must depend on individual circumstances, such as the degree of histological malignancy, the age of the patient, the kind of operation which has been done, etc. For example, there is no doubt that many patients have remained well after supravaginal hysterectomy, especially when the level of amputation has been well below the tumor. Moreover, a considerable proportion of the sarcomas developing in myomas, but not by any means all, are of a relatively low degree of malignancy, certainly considerably lower as a group than the diffuse variety of sarcoma.

If the surgeon is trained in pathology, the probably sarcomatous nature of a myoma can often be strongly suspected at operation, if the tumor nodules are opened before the abdomen is closed, always a wise precaution. If the cut surface is hard, glistening and trabeculated, there need be little fear of sarcoma. If, on the other hand, it is soft and pultaceous, with perhaps one or more ragged degeneration cavities, sarcoma should be suspected and the extent of operation thus indicated.

It is to be remembered that metastases are commonly of systemic rather than regional distribution, as is indicated by those noted in Kardash's cases. With the larger tumors, however, there may also be local pelvic infiltration, so that postoperative pelvic irradiation is usually wise, though it may offer little protection against blood-borne metastases to such organs as the lungs, liver, kidney or brain.

While vaginal bleeding is often a symptom, there are many cases in which it is absent even in large growths. My own most recent case of sarcoma was a huge growth of the diffuse type the size of a watermelon in a patient of 70, which because of its rather unilateral position and the entire absence of any vaginal bleeding, was thought to be an ovarian neoplasm. As a matter of fact, the diagnosis is most frequently made only at operation or later, in the laboratory. In a small group of cases, especially those of endometrial type, microscopic examination of curettings will make the diagnosis. In sarcomas originating in myomas, it is easy to see why even the most thorough curettage will usually fail to yield any cancer tissue.

See also comment on following abstract of paper by Perry.—Ed.)

It is easy to see that I personally do not accept the indispensability of preoperative radiation and do not usually follow the plan in the early cases. In the more advanced cases, in which the uterus is filled with necrotic, infected fungoid tissue, I am more likely to employ preliminary radiation. Speert and Peightal present figures which compare favorably with those of the advocates of the combined plan, although only those for early cases are given.

In the larger teaching clinics it is probably easier to follow the long drawn out combined plan than with private patients, on whom the preliminary radiation imposes the mental anxiety and apprehension entailed by a delay of a couple of months before the operation which still looms ahead. This of course would not be a vital consideration if the advantages of the delay clearly and decisively outweighed the disadvantages, but I for one do not believe that this has yet been established beyond doubt.—Ed.)

SARCOMA OF THE UTERUS. REPORT OF TWO CASES WITH GENERALIZED METASTASIS

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Am. J. Obst. & Gynec., 56: 566-573, 1948

Ten cases of sarcoma of the uterus have been seen in the past 10 years at this hospital. Three were primary and 7 were secondary to myomas. Uterine sarcoma constituted 1.7 per cent of uterine malignancies; 0.48 per cent of the myomas showed sarcomatous degeneration.

The ages in this series ranged from 41 to 74 years, with an average of 52 years. Eight of the patients were married and 6 were known to have borne children. Seven patients presented vaginal bleeding as the chief complaint, and the remaining 3 had pain as the presenting symptom. Nine patients had palpable abdominal and pelvic masses at admission. The diagnosis was not made once in this series and malignancy was suspected only 3 times prior to operation.

Five patients had a supravaginal hysterectomy; one, a panhysterectomy; one, an exploratory laparotomy; one, dilatation and curettage and radium implantation; one, dilatation and curettage and irradiation; and one, irradiation alone. Six patients died within 3 months of their hospital admissions as a result of the pelvic lesions, one died of cardiac disease 20 months after operation, and 3 are alive and asymptomatic at the present time. Of the 3 cases that have come to autopsy, 2 showed generalized metastasis and one, local metastasis.

The two cases of sarcomatous changes in fibromyomas with generalized metastasis are reported in detail. The first patient had metastases to the lungs, liver and right kidney. The second patient showed metastases to the sigmoid, liver and lung.

The author suggests that the early removal of fibromyomas may be advocated, and advises chest x-rays in suspected cases of uterine sarcoma. 6 figures.

which contain a variety of mesodermal elements, such as cartilage or striped muscle fibres, much as does the very rare sarcoma botryoides. These tumors are thought to arise in mesodermal elements pulled down by the Wolffian duct during the period of its embryological descent, though opinion is not unanimous on this point. It is evident that this is not what Perry means, since he includes stromal or "mucosal cell" cancers in the mixed group; just why I do not know. Sarcomas of stromal origin are commonly classed as endometrial. Again, if a cancer arises from mucosal cells it would be considered a carcinoma and not a sarcoma. It is evident that at least one reader is thoroughly confused by Perry's method of classifying uterine sarcoma.

Another surprising finding in this study is that only 1 of this group of 18 cases was found associated with a leiomyoma and that there were apparently 11 cases of "stroma cell or mixed tumors of various types."

See also comment on preceding abstract of paper by Kardash.—Ed.)

THE CLINICAL SIGNIFICANCE OF CHRONIC PARAMETRITIS

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California Med. 68: 159-161, 1948

Chronic parametritis is a condition characterized by a demonstrable thickening of the sacro-uterine ligaments. The author estimates that it occurs in about 6% of all gynecological patients.

A study based on 54 private patients indicated that the maximal frequency was between 25 to 35 years of age, and was more frequent in multigravidae. The most characteristic symptoms are vague lower abdominal pain, dyspareunia, backache, dysmenorrhea, and pain on defecation.

The diagnosis is established by demonstration of a thickening and tenderness of one or both sacro-uterine ligaments which are easily palpated in the presence of an inflammatory lesion. The simplest method is a rectovaginal examination. Endometriosis is a prime consideration in the differential diagnosis. This type of chronic parametritis is a result of inflammatory lesions of the cervix.

Treatment consists of the elimination of any cervical lesions and the use of hot Sitz baths, with continuous douche. Of 33 patients treated, 6 returned with recurrence.

(Chronic parametritis of the degree described by the author is not an extremely common entity, though milder degrees, in which the chief symptom is often dyspareunia, and in which the uterosacral ligaments are only slightly thickened and tender, are much more frequent. The simple plan of treatment recommended by the author will often make the patient reasonably comfortable, and if the chronic cervicitis or erosion is corrected, the symptoms often disappear completely. On the other hand, there is, in a few rather rare instances, usually those of long standing, such an extreme degree of uterosacral thickening and such exquisite tenderness that even hysterectomy must be thought of, and in such cases this should be of the total variety.—Ed.)

SARCOMA OF THE UTERUS

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New England J. Med., 238: 793-799, 1948

A review of 18 cases of sarcoma of the uterus seen at the Rhode Island Hospital was made, with attention given to the pathology of the tumors in order to determine the probable origins and the relation of cytologic factors to the prognosis. A preponderance of leiomyosarcomas, varying between those of low grade malignancy and those anaplastic and rapid, is usually found. Stromal or mucosal-cell cancers are classified as mixed mesodermal tumors containing more than one type of tissue of mesodermal origin and carcinosarcomas containing elements of connective tissue origins and epithelium. Hemangiosarcoma and sarcoma botroides are rare types. All tumors cannot be pigeonholed, as some are too anaplastic.

Classification of the 18 cases was as follows: 7 leiomyosarcomas, 4 mixed mesodermal, 3 carcinosarcomas, 2 giant-cell, one stromal-cell, and one sarcoma botroides.

The results of treatment of the 7 leiomyosarcomas were not encouraging; only 2 of the patients are still living and well one and 4 years after operation, respectively. Bleeding, pain and an abdominal mass were the chief complaints. Panhysterectomy with bilateral salpingo-oophorectomy is considered the treatment of choice. In spite of reasonably prompt surgery, the disease was usually advanced at the time of operation. There was an indication that early lesions have a favorable prognosis.

Evans' theory that prognosis bears a relationship to the number of mitotic figures in a given lesion seems to be supported. Two cases seem to validate the presumption that tumors with few mitoses grow slowly. Only one tumor was found associated with a fibroid, which further supports the view of Evans as opposed to the concept that leiomyosarcomas always arise from a leiomyoma. It seems likely that most tumors are malignant from their inception.

There were 11 cases of stromal-cell or mixed tumors of various types and only 2 are still alive and without recurrence after 5 and 13 years, respectively. These tumors lined or projected into the endometrial cavity. The silent nature of these tumors explains the low survival rate.

Eight patients received radiation therapy of some sort. X-ray seemed to be of little palliative value. One case was favorably relieved by preoperative radium, as evidenced by the presence of necrosis in the pathological specimen.

Cases of leiomyosarcoma with late metastases to the humerus, a mixed mesodermal sarcoma, a carcinosarcoma occurring after radium treatment for menopaual bleeding, and a sarcoma botroides are reported in some detail. 10 figures.

(The fact that 4 of the author's 18 cases are of "mixed mesodermal" type and 3 are carcinosarcomas seems astonishing in view of the great rarity of real mixed mesodermal tumors,

is likely to recur when only one ovary is present, a few years of relief bring the artificial menopause and the climacteric closer together. The author feels that a premature menopause does not terminate until the natural span for the individual has elapsed. Thus, discomfort and instability are intensified. Exploration of an ovary is not difficult and should be part of every laparotomy where this organ can be reached. This procedure is presented as a conservative gynecological measure which can be applied to nonproliferative cysts of the ovary, the most common cause of ovarian failure. 11 figures.

(This is a difficult paper to comment upon (like Winston Churchill, I believe that a proposition often looks happiest and most comfortable at the end of a sentence). The author of the paper has built for himself a rather fine-spun hypothesis, which certainly has not been proved and which I do not think can be proved, but in which he obviously believes so wholeheartedly and so enthusiastically that he makes it the basis for a surgical procedure which I believe will strike most readers, as it certainly struck me, as an ill-advised recrudescence of the tinkering type of ovarian surgery so well exemplified in the resection of "cystic ovaries." The latter practice is happily becoming much less widespread, although it is still among the gynecological accomplishments of a good many of our friends among the general surgeons. Without meaning to be unkind, I feel quite sure that Battey of Georgia was equally sincere in his belief that removal of the ovaries would cure epilepsy, nervousness, headache and many other female ailments, and the Battey operation (Batty could well be spelled with a small b) ran its short, inglorious and devastating career, leaving thousands of removed normal ovaries in its wake. I do not believe that the author of this operation has set forth much more than a hypothetic rationale for the procedure, while on the other hand, everyone who has done many secondary operations in which ovaries have been partially resected has had very good evidence of the possible harm which may follow, especially in the production of intestinal and omental adhesions and other such sequelae. The most important rule in surgery is that simple dictum of Ambroise Paré, "Ne nocere." With full regard for Jacobson's obvious sincerity, I have tried to make it clear that I do not at this writing feel impelled to adopt his recommendations and that any wide adoption of his procedure would add to the health and happiness of womankind.—Ed.)

SOLID TERATOMA OF THE OVARY, WITH REPORT OF FIVE CASES

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Am. J. Obst. & Gynec., 56: 300-310, 1948

The author points out that the differentiation between the cystic dermoids and solid teratomas is often difficult. In addition, the concept that the dermoid is of ectodermal origin no longer seems to be borne out, although these tumors do usually have a preponderance of ectodermal structures. The writer proposes that the word teratoma be confined exclusively to the solid type of tumor and be considered malignant by definition, and that the use of the word cystic teratoma to imply dermoid be discontinued. The differential diagnosis will often

THE ADNEXA

PRESERVATION OF FUNCTION IN CYSTIC AND SCLEROTIC OVARIES

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Petersburg, Va.

Surg., Gynec. & Obst., 87: 31-43, 1948

The author feels that ovaries affected with cystic or sclerotic disease need not be lost, and that it is possible to explore and to improve the utility of the ovary without oophorectomy. In order to prove this, he presents 16 cases in which one ovary and both tubes previously had been removed and on which he performed surgical therapy. His success in restoring ovarian function leads him to believe that here is another aid in preventing wholesale ovarian excision.

Follicles which do not rupture or regress rapidly may impede the cyclic activity of the ovary without ever becoming enlarged. This occurred in all 16 cases reported here. The presence of areas of increased pressure caused by such follicles is easily detected by manipulation of the organ while it is still attached to the body. The tense follicles may be a source of pain, often simulating appendicitis in teen-age girls. Follicles expanding near the white line at the hilum of the ovary often provoke a more intense fibrotic reaction than those at the free ovarian border. The reaction may extend over the entire ovary as well as up into the mesovarium and in the meanwhile squeeze off the blood supply passing through this region. But even an ovary so compressed as to be practically useless may contain many cells capable of being revived.

One ovary is not adapted to the beat of two; thus, when cyclic rotations are taking place rapidly, the ovarian stroma becomes enmeshed in follicles and endocrine inadequacies and discomfort result. After such a condition is well established endocrine therapy has little to offer. Physical forces play a large role in ovulation; the distribution of intraovarian pressures is constantly changing to allow the slow rupture of a follicle. A follicle maturing deep in the ovarian body or between the white lines in the hilum has little chance of rupturing and becomes a static mass which can alter the entire internal structure. Evacuation of these follicles can often restore the blood supply and allow the ovary to function once again.

The technique of the operation is presented in some detail. Examination and straightening of the mesovarium is the first step. Because of its friability the ovary is best held between the fingers and a clamp is not used on the mesovarium, bleeding usually being slight. Figures 5 to 10 picture the ovarian incision and extraction of the follicle.

The operation is not intended as a substitute for endocrine therapy and should not be undertaken until all other measures fail. Even though the abnormality

A PSEUDOMUCINOUS CYST OF THE OVARY WITH ASCITES AND
HYDROTHORAX

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New York State J. Med., 48: 527-528, 1948

A case is reported in which ascites and hydrothorax were associated with a massive pseudomucinous cyst of the right ovary, as the author wishes to stress the fact that a causative agent other than ovarian fibromata was found.

A 34 year old woman was admitted to the hospital because of a markedly distended abdomen. At operation a pseudomucinous cyst of the right ovary was found and removed. Pathological examination revealed no evidence of a malignant character or invasive tendencies. The convalescence was uneventful and the patient later became pregnant.

Cases exhibiting the triad of ovarian tumor, ascites and hydrothorax can easily be confused with ovarian malignancy and metastasis. It is essential that a thorough study of the patient exhibiting the finding should be made before operation is decided against.

(This case report is of interest in view of the friendly controversy which was published in the "Correspondence" pages of the American Journal of Obstetrics and Gynecology in its October issue concerning the propriety or impropriety of including under the designation of Meigs syndrome the cases in which ascites and hydrothorax co-exist with other ovarian tumors than solid fibromas. In this little interchange between Joseph Millett and Herbert F. Simon, it would seem to me that the former, taking the affirmative side, had the better of the argument. The syndrome has been reported with cystadenomas of either pseudomucinous or serous type, carcinomas, granulosa or thecomatous tumors, and Brenner tumors, as well as fibromas. So far as we know, the mechanism is exactly the same, though no one knows exactly what it is. It goes without saying that the syndrome designation should not be applied where the hydrothorax is due to actual pleural metastasis of malignant tumors. Rosenfeld's report adds another case to the now considerable group in which the syndrome has been present with ovarian tumors other than fibromas, of which it was at one time thought to be characteristic.—Ed.)

be based solely on the histological appearance of the tumor, though in borderline cases even here there may be divergence of interpretation.

The author reports 5 cases in detail. Two of these cases were found in a total of 35,000 admissions to the gynecologic service at Johns Hopkins Hospital over a 20-year period. Two cases were seen at the Harriet Lane Home for Invalid Children and one was seen in private practice. Four of the cases followed a typical course. Though the duration of symptoms was short, the tumor was far advanced. The average age in these 4 cases was 26 years. X-ray therapy did not seem appreciably to alter the course in any of these cases. The histological pattern in each instance was that of a highly undifferentiated, disorderly malignant type of tumor.

The fifth case survived after operation. This tumor was submitted to the Ovarian Tumor Registry for consideration by 5 experts; two members called it simple teratoma, one called it teratoma benign, another designated it as teratoma (embryonal) and the last considered it to be a dermoid cyst. In this case the cells were highly differentiated, and there was a fair, though imperfect, attempt at actual organ formation. It seems apparent that the word teratoma has a diverse connotation to different individuals, and this last case illustrates the confusion on this point, even among trained pathologists.

(The author's proposal that the term teratoma be applied only to the solid malignant tumors made up of tissues alien to the ovary and commonly showing derivatives of all 3 fetal layers, seems to me to be a sound one, largely because it is in conformity with general usage. It is of course true that a simple dermoid, made up dominantly but not always exclusively, of ectodermal elements, also conforms to the pathological definition of teratoma, and that the pathological purists have a case in urging that the term dermoid be replaced by that of cystic teratoma. But there is another difference in the two groups, for in the solid teratoma the tissues are of unripe type with wicked clinical potentiality, while in the other the alien elements are well differentiated, with therefore absence of clinical malignancy.

In any event, the use of the term dermoid for the cystic, benign, largely ectodermal tumors, has become so firmly established by long usage that it would probably be as difficult to dislodge as the common employment of the term fibroid for a uterine myoma. The literature of pathology, like the English language in general, is full of inconsistencies and inaccuracies in nomenclature, and the way of the reformer has always been a hard one, and almost always unsuccessful. Whether right or wrong, I believe that most of us know what we mean when we speak of a simple dermoid, and what is suggested by the term solid teratoma, and perhaps we ought to reconcile ourselves to them rather than confuse the literature with a new nomenclature which in itself is not free of vulnerabilities.

The author's gentle little crack at the 5 supposed experts in gynecological pathology who make up the Ovarian Tumor Committee of the American Gynecological Society leaves me cold. They get a lot of weird tumors to study, and it is not surprising that at least in a small proportion their diagnoses are also weird and divergent, on grounds much more substantial than mere nomenclature. I believe that with one baffling tumor 6 different diagnoses were submitted by the 5 men of the Committee. In defense of the Committee, however, I may say that in the overwhelming majority of cases, the opinions of this group exhibit a rather remarkable degree of concordance.—Ed.)

ment of urethral cancer is usually a difficult problem. Surgical excision of the early types is feasible, but it should be as wide as possible, and often involves removal of the vesical neck, while the inguinal glands should likewise be removed. Considerable plastic ingenuity may be necessary to preserve sphincter control. In the more advanced stages radiotherapy will most often be resorted to.—Ed.)

EPITHELIAL METAPLASIA OF THE URINARY TRACT

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Montreal, Canada

J. A. M. A., 136: 824-827, 1948

The finding of tissue cells of another type than that normally found in an organ gives rise to difficulty in explanation as to the mechanism by which such metamorphosis has been produced. Such changes are not unusual in the urinary tract: in the renal pelvis, the ureters, and the bladder, which are lined with transitional cell epithelium and in which glands are not present.

Metamorphosis of this epithelium is of 2 types: 1. the substitution of stratified keratinizing epithelium and the development of leukoplakia and finally squamous cell carcinoma, 2. the appearance of glandular formations with secretory properties, the cystitis glandularis and finally 3. a mucin-secreting adenocarcinoma.

Leukoplakia is noted less frequently than squamous cell carcinoma and both are more often met in the bladder than in the renal pelvis and the ureters. Most authors have agreed that leukoplakia is metaplastic in origin. It is associated with longstanding irritation and inflammation. It has also been shown to follow fat-soluble Vitamin A deprivation in animals and upon restoration of diet it is replaced by normal epithelium.

Leukoplakia is considered a precursor of squamous cell carcinoma. In 1929 the author collected 13 cases in which the 2 conditions were associated and other such cases are reported in schistosomiasis of the bladder. Intermediate processes between the 2 conditions have been demonstrated by the author and his colleague, Dr. Rhea, by means of serial sections. These, if not definitely malignant, were certainly precancerous. In these cases there is no benign stage but acceleration of the metaplastic and development of malignancy.

Recent observations have led to the conclusion that cystitis glandularis and mucin-secreting adenocarcinoma are metaplastic in origin also. The glandular formations develop from epithelial cell nests of von Limbeck and von Brunn as a result of chronic inflammation. The process is a secreting one. This process has been reproduced experimentally by introducing foreign matter into the bladder of a rabbit. If the stimulus which initiated the process of adaption becomes inert the process may be retarded and an impotent cyst remain. Such cysts are frequently found in the renal pelvis and the ureters. Contrary to

FEMALE UROLOGY

THE RELATIONSHIP OF URETHRAL CARUNCLE TO CARCINOMA OF URETHRA

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Montreal, Que.

Canad. M. A. J., 58: 373-376, 1948

The present concept of the nature of urethral caruncle has undergone considerable change since the recognition that a malignant process not infrequently underlies this seemingly benign exterior. Other investigators have found as high as 40 per cent of these lesions to be malignant on pathological examination.

Clinically, the caruncle appears as a soft, reddish, sensitive excrescence occurring usually on the posterior lip of the urethral meatus. It may be pedunculated, tends to bleed easily and is often sensitive to touch or the flow of urine. The histologic picture is that of chronic inflammation. The presence of cancer in such a lesion can often be undetected by gross examination, section and histological study being necessary in order to arrive at this conclusion. The etiologic basis of caruncle is controversial; however, the authors feel that chronic inflammation plays an important role. The most common symptoms are pain, frequency, burning on urination, and bleeding, though occasionally the lesions may be entirely asymptomatic and are only discovered on pelvic examination.

A case is reported of a 49-year-old white female who complained of painful urination, urgency, frequency and itching of the vulva of 2 years' duration. There had been occasional episodes of blood-tinged urine. On pelvic examination, a soft, red tender mass, 0.5 cm. in diameter, was noted on the posterior lip of the urethral meatus and protruding slightly from the orifice. The lesion was excised completely with the electro-cutting knife. Pathological examination revealed a well differentiated squamous cell type of carcinoma. The lesion was apparently limited to the caruncle, though a few nests of epithelial cells were found extending down into the underlying stroma.

It is felt that the urethral caruncle is a precancerous type of lesion which often becomes frankly carcinomatous. One can readily see the necessity for complete excision of the urethral mass, once treatment is undertaken, and multiple sections should be studied for malignant changes. Superficial cauterization with caustics such as silver nitrate may well be responsible for the failure to identify early urethral carcinoma; the patient thus misses an opportunity for prompt treatment.

(There is no doubt that urethral carcinoma is preceded by caruncle in a considerable proportion of cases. On the other hand, carcinoma of the urethra is rare and caruncle is common, so that the actual incidence of malignant change in caruncles is low. The treat-

OPERATIVE GYNECOLOGY

GYNECOLOGIC SURGERY IN THE ELDERLY WITH SPECIAL REFERENCE TO RISKS AND RESULTS

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Am. J. Obst. & Gynec., 56: 440-456, 1948

The increasing numbers of elderly women presenting a variety of gynecologic disorders bring new responsibilities to the gynecologist and to the internist. The present study concerns 217 gynecologic operations which were performed upon 202 women over 60 years of age from January 1, 1941, to December 31, 1946. The procedures included 44 laparotomies, 10 vaginal hysterectomies, 67 vaginal plastic repairs, 5 vulvectomies and 91 minor operations.

There were 84 cases of vaginal lesions associated with relaxation of pelvic supportive structures, evidence of the importance of the loss of elasticity in aging tissues. The occurrence of uterine fibroids producing symptoms in older women (7 cases) illustrates that all fibromyomas do not recede after the menopause. There were 34 benign endometrial abnormalities associated with bleeding, in contrast with an identical number of cases of malignant uterine disease. There were 19 benign ovarian lesions and only 7 malignant ovarian lesions.

The predominating symptoms were vaginal bleeding (88 cases) and subjective sensations of protrusion at the vulva (67 cases). Uterine bleeding was associated in 42 cases with benign lesions and in 35 with malignant changes. Fourteen of the cases of benign uterine bleeding were due to uterine polyps, 6 of the patients being over 70 years old. It is shown that in nearly one-half of the group of cases of pelvic relaxation, the aging process may be considered as a determining factor in the production of active symptoms.

These elderly patients presented a variety of systemic conditions associated with the local lesions. The implications of hypertension, arteriosclerotic heart disease, anemia, diabetes and malnutrition are discussed in relation to the determination of surgical risk. The authors believe that chronological age is of importance only in emphasizing the need for careful general medical examination. Preoperative elimination of possible sources of difficulty during operation and the postoperative period includes improvement of nutrition, treatment of anemia and hyperglycemia, glycosuria and ketosis, support of the cardiovascular system, eradication of infection by means of antibiotic therapy, and systematic psychotherapy to assuage fear and apprehension.

Modern methods of anesthesia, liberal use of whole blood transfusions, early rising, and the use of chemotherapy and antibiotics prevented or modified complications of the postoperative period. Ethylene proved very satisfactory

textbook statements the author believes the instances of adenocarcinoma in the urinary tract rare.

An adenocarcinoma results from an acceleration of the metaplastic process. Sources of chronic irritation such as schistosomiasis and exstrophy of the bladder are important factors in the pathogenesis of this condition as well as cystitis glandularis. The cystic and glandular formations may disappear when the inciting irritation or infection is removed.

Epithelial cells of the urinary tract possess latent potentialities of proliferation which on irritation may be followed by unrestrained growth. This change in the character of the cell may cease to be active or may be reversed.

CONTRACTURE OF THE VESICAL NECK IN FEMALES

L. B. SCHUMAKER AND F. C. HENDRICKSON

Canton, Ohio

Urol. & Cutan. Rev., 52: 205-206, 1948

Fifteen cases of transurethral resection of the internal sphincter in women have been presented by the authors. There are several etiologic factors involved which may be responsible for incomplete emptying of the bladder in the older female patient, but by far the most common cause is contracture of the vesicle neck. This may be secondary to congenital hypertrophy of the vesical sphincter, injury sustained during childbirth or chronic infection of the urethra.

Certain cases may respond to dilatation by sounds and all cases deserve a therapeutic trial by sounds before operation is advised. The operation is performed by making longitudinal cuts with a resectoscope to a depth of about 5 mm. and extending entirely around the internal sphincter. The cuts are extended distally about 7 to 8 cm. Prior to operation the internal sphincter is infiltrated with 50 cc. of novocaine. This is done to thicken the urethro-vaginal septum and so reduce the danger of vesicovaginal fistula.

Results in these cases have been as follows: 8 cases were cured, 6 were improved and one was unimproved. The average residual urine before operation was 200 cc. and that after operation was 40 cc. No serious complications were encountered.

cardiopath. Renal function can be determined by a specific gravity test. Pulmonary emphysema, chronic bronchitis, diabetes and nervous complications must be evaluated.

In immediate preoperative preparation, sedation should not be too great as the elderly patient is more easily depressed; hence, barbiturates and demerol are preferable. Intravenous pentothal is unsafe because of the greater retention of drugs. Procaine anesthesia is best tolerated by older people. Of the gaseous anesthetics, cyclopropane with high oxygen content is best.

The operative procedures must be rapid and precise with the least shock-producing manipulations. Vitamin C and estrogenic hormones are aids to healing. Immediate postoperative treatment is important. Protection against cooling of the body, frequent changes in position, oxygen inhalations, intravenous fluids, blood transfusions, and finally, early ambulation are methods of preventing complications.

Thus, surgical risk can be maintained at a minimum, and relief to an elderly patient with a good life expectancy more than balances this risk.

(The observations and the advice embodied in this paper, as well as in that of Zeman and Davids, are sound. It is interesting and sometimes amusing to see how differently surgeons, as well as people in general, evaluate such descriptive adjectives as "elderly" and "old," the influencing factor in these varying viewpoints being often the age of the person using the terms. I remember that last year this elderly Editor had some fun chiding the callow author of a paper on surgery in the aged, in which group were placed all patients over 50.

A considerable proportion of the patients in any gynecologic clinic are over 60, and this certainly applies to those with various types of genital prolapse. I have seen surgeons do Leport operations on patients still in their 50's, when the prolapse could have been safely and expeditiously corrected under local anesthesia. The value of local anesthesia in plastic surgery in old patients is not sufficiently appreciated. Many women of 70 are still in good general condition, and I do not think that they need always be consigned to a pessary life, or even to the Leport type of operation. In a good many cases local anesthesia permits of safe correction procedures, especially when combined with early ambulation. There can of course be no generalization on this point since the physical status of many women much less than 70 should lead one to resort to conservative plans of treatment, often nonsurgical. The point is that the mere chronological age, as the authors emphasize, should not play too decisive a role.

As a matter of fact, it is surprising how well most of these older patients, when properly selected, do after operation. The authors of both papers give good advice on the importance of selecting the proper anesthetic, especially in the abdominal group, where the indication for operation is often more pressing than in the vaginal group, as in the carcinomas of the ovary often seen in old women. These are not ideal cases for the dawdling type of surgeon, as these operations should be done as expeditiously as is consistent with thoroughness.—Ed.)

as an anesthetic for older patients. Demerol may be effectively substituted for morphine as preanesthetic medication in elderly people.

Postoperatively, there were 4 minor wound infections. Four cases of pyelonephritis occurred which responded promptly to treatment. Three cases of thrombophlebitis occurred. Four cases developed bronchopneumonia following operation; three of these recovered promptly with antibiotic therapy. One patient with inoperable carcinoma of the ovary developed bronchopneumonia and died. Another patient, operated upon for carcinoma of the fundus, died of massive pulmonary embolism.

The writers conclude that the careful evaluation of the functional capacity of older individuals will eliminate false emphasis on chronological age, and thus point the way to successful therapy.

(See comment on following abstract of paper by Lash.—Ed.)

GYNECOLOGICAL SURGERY IN THE ELDERLY WOMAN

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Geriatrics, 3: 67-71, 1948

Attention is called to statistical evidence of the prolongation of life in this country, producing a large population past 60 who require special medical attention and deserve to be active members of society. Gynecological conditions requiring surgery have been treated incompletely and palliatively in the past because of the patient's age. The author believes this attitude to be wrong and feels that operative mortality is not higher from surgery per se but from the medical condition or pathology present. The pelvic conditions in elderly women requiring surgery, i. e., pelvic herniosis, and benign and malignant tumors, can be approached today with confidence because knowledge of preoperative and postoperative care as well as anesthetic and surgical technique have been so advanced.

A plan of preoperative study is suggested. First, an important reassuring talk should take place with the patient about her condition to determine her attitude towards the operation. This is particularly important in treating the elderly patient whose will to live may not be strong. Second, a determination of physical defect or degenerative disease present must be made. Transfusions and large doses of vitamins are helpful in preparing the patient for surgery in a short time. All foci of infection should be eliminated. The adequacy of the cardiac reserve and coronary arterial sclerosis can be studied by roentgenography and electrocardiography. Anesthesia must be considered in the hypertensive; local, regional, or low spinal will be well tolerated. A spinal is best avoided in

STERILITY

INFERTILITY OR STERILITY IN THE FEMALE

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M. Clin. North America, 32: 37-56, 1948

The childless family is an important medical and sociological problem. It is estimated that somewhere between 15 and 20 per cent of all marriages are childless involuntarily. In most cases it is now possible to determine the cause and at least one-third of the couples who are subjected to sterility work-up ultimately have children.

No arbitrary time can be selected following which the couple can be considered sterile; a patient is entitled to a study no matter how long she has tried to have children. But much more can be done with young women. Contraception for child-spacing does not decrease fertility, but too long a delay in raising a family may decrease fertility as the early 20's are the most fertile years.

The physician should encourage the examination of the couple rather than the wife alone. In one-third of the sterile couples the husband is responsible and in another third he is a contributing factor.

Several organic factors influence fertility. Normal anatomic structures are necessary for reproduction. Failure of embryonic fusion may result in a complete duplication of the reproductive tract which can influence fertility to some degree. Where one segment of the tract has failed to develop, as in the absence of the vagina or uterus, pregnancy is impossible. Disease may alter the organs and interfere with fertility. Infection resulting from gonorrhea, abortion or childbirth may alter the fallopian tubes by interfering with the patency of their lumens. About 5 to 10 per cent of upper genital infections are tuberculous in origin and destroy fertility. In the lower tract trichomoniasis, monilial vaginitis and such infections reduce fertility. Malpositions of the uterus are of no great importance, as in about 15 per cent of normally fertile women the uterus remains retrodisplaced.

The reproductive organs must function normally if conception and normal pregnancy are to take place. The production of normal ova by the ovary, the rupture of the follicle, the transportation of the egg down the fallopian tube, fertilization and consequent implantation in the endometrium of the uterine cavity, all this must occur properly. Ovarian changes must be initiated by the follicle-stimulating gonadotrophin and the luteinizing gonadotrophin hormones. Changes in the endometrium necessary for implantation of the fertilized ovum are controlled first by the estrogenic hormone and later by progesterone. Coitus must take place within 24 to 36 hours of ovulation as the life span of both sperm

PERINEAL DISSECTION FOR REPAIR

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Charleston, W. Va.

Am. J. Obst. & Gynec., 56: 509-514, 1948

The writer discusses several points which simplify perineal dissection for repair. First, a large, 4-inch long and one inch in diameter rectal dilator is inserted into the rectum as the first step of the operative preparation and is retained throughout operation to facilitate dissection and tissue identification and suturing.

Local injection left and right about the levator muscles of 30 cc. of normal saline solution with Adrenalin (3 drops) is employed for hemostasis and partial dissection.

Dissection of the levator ani muscles is the first step in the operation, through one-inch, bilateral stab wounds. The main part of the dissection is thus accomplished quickly and easily in nontraumatized, less vascular, less adherent structures from above downward. The proper plane for dissection is easily found and followed. There is less danger of invading the rectum.

This technique reduces operative time and is especially adaptable for postpartum perineal repairs. 7 figures.

(While there can be no objection to the 3 points of technic advocated by the author, I do not believe that they will have any general appeal, chiefly because they make of the ordinary posterior repair a more elaborate procedure than it usually is. The employment of a large rectal dilator would not seem necessary to facilitate identification of the perineal structures, nor should the injection of normal saline solution with adrenalin. Incidentally, the latter procedure is much more valuable in operations for cystocele and prolapse, especially when local anesthesia is being used. Personally I do not use the method as a routine in association with general anesthesia, as some gynecologists do, but in operations such as vaginal hysterectomy in elderly women the addition of a few minims of adrenalin (some use posterior pituitary extract) to the novocain used for local infiltration is, to my mind, a valuable aid in hemostasis as well as tissue plane differentiation.

Finally, it is my belief that the majority of gynecologists no longer dissect out the muscle tissue of the levators, but depend upon approximating sutures passed deeply through the levator fascia. To dissect out the muscle fibers through incisions in the fascia, as the author describes and as was more often practised in the earlier days of the procedure, has the disadvantage of taking longer and of not infrequently being followed by dyspareunia from the band of approximated muscle tissue. Moreover, it is not necessary, as very satisfactory results are obtained without including it in the operative technic.—Ed.)

impossible. A salpingostomy may occasionally be done in cases of tubal blockade. Where there is complete sterility in the husband, artificial insemination is a possibility. Ovarian failure is usually a complete barrier to childbearing. In such cases of complete sterility the author believes that the patient should be informed of this and should be urged to consider adoption or some such alternative. 9 figures.

(Although it introduces no new concepts, a rather full abstract of this paper is published because it presents a simple but rather complete summary by a competent investigator of accepted views and practices concerning this problem. Gynecologists will of course differ somewhat on certain points, as for example their preference for salpingography or tubal insufflation as the favored routine method in the study of tubal patency. Again, many utilize basal temperature records as practically a routine while others limit their use to certain groups of women, especially those with very irregular cycles. Incidentally, a collective review of the subject of basal temperature studies in relation to menstruation, ovulation and pregnancy, from the pen of a leading advocate of the method, is published in the present issue of the Survey.—Ed.)

STERILITY IN THE FEMALE

K. M. GRANT

Halifax, Nova Scotia

Am. J. Obst. & Gynec., 55: 416-424, 1948

The author intends to outline a reasonably thorough and effective plan for the investigation of a sterile couple and for treatment where indicated. He emphasizes the necessity for the study of the husband as well as the wife.

Three conditions must be obtained before pregnancy can occur. One, healthy sperm must be deposited at the cervical canal. Two, the sperm must be able to ascend and fertilize a healthy ovum and three, the ovum must implant on prepared endometrium.

It is necessary to maintain a balanced outlook in the investigation of sterility; laboratory methods must be incorporated with the investigation of the reproductive tract and the clinical examination of the patient as a whole. The author believes that it is usually possible to carry out the investigation in 3 office visits or less.

At the first visit a complete medical and gynecological history is taken. A complete physical examination including routine blood tests and urinalysis is done. Clinical evaluation of endocrinological stigmata is made. A pelvic examination is done with particular attention given to infections of the lower genital tract. The treatment of vaginal discharges of known etiology is advised. The author finds that probing the cervical canal with a uterine sound has remarkable results. He also feels that whereas retrodisplacement of the uterus has been

and egg do not permit fertilization after this. Normally the cervical mucus becomes more penetrable and favorable to sperm at the time of ovulation. The author wishes to emphasize the fact that reproduction is dependent on an intricate and carefully timed mechanism recurring cyclically. Any abnormality of structure or function can reduce fertility or result in sterility.

Thus the author's sterility studies consist in evaluating organically and functionally the normalcy of the reproductive tract and the stimulating glands. The husband must also be studied in this manner.

A careful history, noting delayed puberty or irregular menstruation, pelvic infection, important medical complications and surgical procedures, is taken. The physical examination should include a complete medical survey as well as a pelvic examination. The cervix particularly deserves study as to its structure and the consistency of the cervical mucus.

It is desirable to visualize the reproductive organs and to establish their patency by means of x-ray. This can best be done the first few days after menstruation. Pressure under which the oil enters the uterus should be controlled accurately. Roentgenograms should be taken as soon as the tubes are visualized, before too much spill has occurred. Patient should return on the following day for second filming. Pelvic inflammation and infection of the lower tract are contraindications to salpingography.

The next step is the study of the ovarian function. Ovulation can be demonstrated in several ways. Endometrial biopsy at the time of menstruation would show the peak of the progestational phase if ovulation had occurred. A study of the progesterone metabolism can be done by the quantitative determination of pregnanediol in the urine. Both of these methods are laborious and indirect, however.

Recently the influence of ovarian activities on the basal body temperature has been adapted to denote ovulation. By graphing temperature taken orally upon awaking, a curve is obtained which is low during the first half of the cycle and is raised by follicle rupture and corpus luteum formation as much as 0.6 to 1.0 degrees above the low point. It will remain high until shortly before menstruation. The period of temperature change is the fertile period in which conception can take place. An accurate record kept over several months is indication of the ovulatory pattern.

A basal metabolic determination should be a part of every sterility study.

The author divides his cases into 3 therapeutical groups. In about one-third of the couples both partners are normal. A temperature graph and the timing of coitus to the period of fertility is recommended as well as a program of general physical and mental hygiene. Pregnancy usually occurs in about 6 months.

The second group includes those with partial barriers to conception. Low fertility in the husband, infections in the lower genital tract and endocrine deficiencies may all contribute to a state of infertility. All factors which can be corrected should be treated after careful evaluation by the physician of their part in infertility.

The third group of couples have insuperable factors which make childbearing

ing present in more than half of the cases examined. Endometriosis of the tube was far more frequent in cases of multiple myoma than in instances of solitary myoma. Sterility may also be caused by the myoma itself because of deformity of the uterine cavity due to location and size of the tumor.

Myoma and adenomyosis often coexist. The 2 chief symptoms are menorrhagia and metrorrhagia. The former is partly explained by the increased amount of endometrium, but more often is due to ovarian dysfunction.

In treatment, radical extirpation of uterus and ovaries has been the rule with few exceptions; myomectomy, though a comparatively uncomplicated operation, is seldom done. In 1922 Mayo reported 909 myomectomies from the Mayo Clinic with 3 deaths and a recurrence rate of 2.5 per cent. Miller reported one death in 141 myomectomies, and 36 per cent of the patients under 38 years of age subsequently bore children.

In performing a myomectomy, it is important to open the uterine cavity. Its omission may result in a small fibroid, polypus or endometrial thickening being overlooked, and menorrhagia continuing after operation. Also, it is much easier to detect fibroids deep in the uterine wall if felt for with the finger inside the cavity. It is absolutely necessary to remove all seedlings.

Conservative operations for fibromyoma, strictly indicated and performed during pregnancy, are not necessarily to be blamed for abortion, if such occurs. Spontaneous uncomplicated births are not usual in women with fibromyomata.

The fully active ovary exercises no less than 7 functions: (1) development of female physical and psychologic characteristics; (2) governs menstruation; (3) produces ova; (4) exercises strong influence on sex-sense; (5) promotes nidation; (6) is largely responsible for breast changes in pregnancy; and (7) is a factor in nervous and vasomotor system control. With these facts in mind, the author states that conservative treatment is too obvious to require further comment.

Enucleation is applicable to all undoubtedly innocent and solid growths in women under 50 years, provided the tumors are not inflamed, markedly adherent or have undergone torsion.

Benign ovarian tumors may be non-neoplastic and neoplastic. There are 4 types of non-neoplastic cysts: the follicle, the corpus luteum, the germinal inclusion and the endometrial. Important neoplastic cysts are: pseudomucinous or pseudomyxomatous cystadenoma, serous cystadenoma, and dermoid cysts. Secondary malignant change may occur with any of the benign neoplastic cysts.

Endocrine function may be ascribed to granulosa cell carcinoma and the closely allied thecoma and luteoma, arrhenoblastoma, adrenal tumors of the ovary and struma ovarii.

The polycystic ovary is a disease entity. If such ovaries are removed conservatively by removing the affected parts, recurrence may never take place and the remaining ovarian tissue probably will function normally.

Hurtado states that a large number of cases of female sterility are produced by sclerocystic degeneration of the ovaries.

Ovulation may fail because of thickening of the ovarian cortex or adhesions. Removal of this thickened capsule may permit normal ovulation.

over-emphasized in sterility, endometriosis is often overlooked and is a frequent cause of sterility.

Instruction is then given the patient as to how to keep a chart recording vaginal or rectal temperatures, the menstrual days and coitus. She is asked to keep this for at least 2 cycles.

Before the next visit a complete history is obtained from the husband and a sperm analysis is done.

For the second visit, if all the above tests and findings are satisfactory, a basal metabolic test, tubal insufflation, and if necessary, uterotubograms are done. The author usually has the patient enter the hospital for a short time to have these tests done. He believes that injection of a radiopaque liquid into the tubes for x-ray can often have a therapeutic effect. If the tubes are found to be patent, the patient is asked to return for a Huhner test.

The third visit is made within 1 or 2 hours after coitus and an examination of the semen from the vaginal pool and the cervix is made. The completeness of the investigation will of course vary with the findings. Absolute sterility when found is an indication to discontinue the study.

Six months should be ample time to investigate a case. Patients lose interest in their cases if asked to return in 6 months after each bit of investigation is carried out.

(See comment on preceding abstract of paper by Davis. The paper of Grant presents a reasonably complete plan of sterility study, practical because not over-elaborate. I was interested in the report of remarkable results from "probing the cervical canal." There is at least some experimental evidence that dilatation of the canal may bring about pituitary stimulation, but whether simple probing would do so I do not know. I suppose that it is on some such basis that the author employs the method, but it would seem that it might be difficult to credit it with any of the remarkable results which he mentioned.—Ed.)

STERILITY AS RELATED TO BENIGN LESIONS OF THE UTERUS AND OVARY

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Am. Practitioner, 2: 374-378, 1948

Uterine myomas may be cervical or corporal, important as related to sterility, either as an endocrine dysfunction interfering with normal function of the endometrium, or as mechanical obstruction interfering with normal migration of ovum or sperm. Fibroids are not necessarily incompatible with pregnancy, but do favor abortion.

Huber (1939), in a study of 432 myoma cases, found that the most frequent cause of sterility, in the presence of myoma, is endometriosis of the tube, a find-

mental hospitals. Their life expectancy is not as long as that of the average person.

There is some evidence that removal of the cause of sterility will help to keep some marriages together and increase the happiness of the partners.

(Important as childlessness is as a prime factor in marital infelicity, I confess I would not have estimated that as many as 71 per cent of childless marriages end in divorce, although I suppose that the author has looked up reliable statistics on this point. On the other hand, I have often been impressed with the love and sympathy for one another of childless couples. So often have I heard the wife express a hope that the examination of her husband will reveal no important defect, as she fears that this would make him unhappy and depressed. Conversely, most husbands I have encountered manifest a sympathetic rather than a bitter attitude toward the wife who has been found sterile. The variants in the psychological reaction of sterile couples to this problem, like so many of married life, are largely those of intellectual and moral fiber, as well as social status.—Ed.)

Sterility is frequently associated with bilateral polycystic ovaries. Surgery may result in a cure.

(This paper comprises a brief discussion of a wide variety of lesions which may be associated with sterility or at least relative infertility. The statement quoted by the author that in more than half the cases of myoma associated with sterility, endometriosis of the tube is found as the important factor, appears to me a rather surprising one. This has certainly not been our observation.

While there are some surgeons who are enthusiastic about myomectomy and some, like Bonney, who seem to me to carry it to extremes, it is done far less often than it should be, especially in the case of women anxious for children. Just why the presence of a myoma imposes at least a relative infertility is not clear, but I am convinced that it does. Every one who does any number of these operations on previously sterile women must have been impressed, as I have been, with the relative frequency with which pregnancy occurs after removal of the tumor or tumors, with sometimes such promptness as to leave little doubt as to the causal role of the tumor.

In doing myomectomies I do not think it is always necessary to open the uterine cavity, although there should certainly be no hesitancy in doing so when there are reasons for doing so. The author states that it is absolutely necessary to remove all seedlings, but, as these are not infrequently microscopic, this is not always possible. There is of course always the possibility of later development of other growths, but if the woman is lucky enough to have a baby or two in the meantime, she is usually willing enough to take this chance, and a later hysterectomy will not be nearly as tragic to her as if it had been done initially.

The term polycystic ovary may mean different things to different surgeons. To many it means only an ovary containing many cystic atretic follicles, usually of small size. Such follicles often come and go, since they always tend toward obliteration. Such ovaries should in most cases not be molested, as they produce no symptoms. In other cystic ovaries, such as those sometimes seen with functional bleeding, the tiny follicle cysts are still actively functional, but the ovarian changes are simply the ovarian expression of the pituitary dysfunction which is the underlying cause of the bleeding, and resection of such cystic ovaries does little or no good, and sometimes harm. There are still other mechanisms involved in the production of cystic ovaries, my point being that the polycystic ovary is not a sharp disease entity, and that it certainly does not always call for resection.—Ed.)

INFERTILITY AND THE STABILITY OF MARRIAGE

P. POPENOE

Los Angeles, California

West. J. Surg., 56: 309-310, 1948

All studies agree that most couples that go into divorce courts are childless. The chances for childless marriages to end in divorce are 71 out of 100. Why are these couples childless? Half of the childlessness is voluntary. Some of the parents involved in these marriages are so inferior in important ways that their childlessness is desirable both socially and eugenically. Statistics show that the group of the childless divorced are more likely to be committed to prison or

future or not. I wonder how women will take to such an idea, or whether it will appeal to the profession, since the simpler types of relaxation, the ones for which it might theoretically be of some advantage, often need no treatment or else are very satisfactorily corrected by very simple surgical procedures. Relaxations may involve actual laceration as well as simple muscle laxness, and here the value of such an appliance would seem to be much less. Finally, in relaxations associated with cystocele, rectocele or uterine prolapse, the group for which most operations are done, I cannot believe that the author's instrument would have much value.—Ed.)

EMBRYOLOGICAL DEVELOPMENT OF THE LEVATOR ANI MUSCLE

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Am. J. Obst. & Gynec., 55: 367-380, 1948

The vulva sphincteric musculature derives its origin from the common cloacal sphincter to which the levator ani is inextricably related as both are ultimately derived from the third and fourth sacral myotomes. The author discusses the development of the vulval sphincteric musculature.

The levator ani muscle is an evolutionary product representing the caudal flexor, abductor musculature of the tailed mammals, which in man has gained new relationships with the pelvic viscera.

The levator ani muscle as shown by its nerve supply is undoubtedly derived from the fourth sacral myotome. The author suggests that as this myotome migrates ventrally it divides into two portions; the iliococcygeus, a continuous sheath, and the ventral longitudinal column, the pubococcygeus. This view means that the structure of this muscle presents analogies with that of the anterior abdominal wall muscles.

The author feels that not enough study has been done on human embryos as yet, but gives several other indications supporting his view.

(The author of this paper has published a number of previous worthwhile anatomic studies, and the one abstracted above, based as it is on embryologic considerations, will be of interest to those interested in the anatomy of the pelvic floor.—Ed.)

MISCELLANEOUS

PROGRESSIVE RESISTANCE EXERCISE IN THE FUNCTIONAL RESTORATION OF THE PERINEAL MUSCLES

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Am. J. Obst. & Gynec., 56: 238-248, 1948

By present standards of obstetrics, it is no longer enough merely to keep the mother alive; it is important to preserve for her the function of her reproductive system. A restudy of the problem of the lax perineum in relation to modern concepts of muscle-cell regeneration and function reveals that the birth canal musculature is especially responsive to an improved method of conserving and restoring function.

The passage of the fetus through the birth canal during delivery is invariably attended by some muscle injury. Excessive tension severs motor end plates attached to muscle cells from the terminal nerve filaments to which they are normally connected. This partial loss of innervation is in large measure responsible for the relaxation of the perineal muscles, but this is not necessarily accompanied by total loss of muscle function. Reinnervation of injured muscle cells can often be stimulated by active exercise and demand for use. The shorter the time lapse between muscle injury due to childbirth or a surgical procedure and the beginning of exercise, the less tissue atrophy occurs and the shorter will be the time necessary to re-establish normal function.

The author has suggested the use of a "perineometer" as an aid in conducting perineal exercise. This is an instrument devised to register muscle contractions and serves as a visual aid to guide the patient during her course of exercise. It has been found useful in restoring function and tone in the immediate postpartum period, improving early cystocele and rectocele during the childbearing years, improving vaginal muscles so that a contraceptive diaphragm may be retained and relieving stress incontinence. Surgical procedures for the correction of vaginal, urethral and rectal incompetence may be facilitated by preoperative and postoperative exercise which improves the texture, tone and function of the perineal muscles.

(I have had no opportunity of observing this interesting instrument in operation, although I suspect it would be a worthwhile spectacle to see a woman exercising her perineal muscles in the manner described by the author, striving mightily to send the registering needle just a bit higher. A good commercial name for the machine would be "Excelsior." Whether or not a patient could overdo her training and become perineally muscle-bound, I do not know. One can think of various horrendous coital casualties which might thus ensue.

These inviting pleasantries aside, I really do not know whether the perineometer has a

picture of many gynecological conditions by permitting visualization of the histopathology of the lesion described. By drawing on his extensive experience and abundant supply of tissue specimens in gynecological pathology, the author has been able to exercise careful selection in presenting photomicrographs of histopathology of the various diseases. The reader, therefore, receives verbal and visual instruction in both gynecology and gynecological pathology.

The last chapter entitled, "Common Disorders of the Female Urinary Organs," was written by Houston S. Everett. The contribution of this experienced author adds materially to the general usefulness of the book and aids in the understanding of urinary problems commonly encountered in the field of gynecology.

NORMAN F. MILLER, M.D.

BOOK REVIEW

TEXTBOOK OF GYNECOLOGY; III Edition; 1948, 742 pages; by Emil Novak, M.D., F.A.C.S. Publisher: The Williams & Wilkins Co., Baltimore, Md. Price \$8.00.

The third edition of this text on gynecology by Dr. Emil Novak, famous American gynecologist and distinguished author, is presented in the same understandable, easy to read, practical manner characterizing so many of his contributions to medical literature.

The sequential arrangement of material is logical and includes consideration of such basic and fundamental things as history taking and the technique of pelvic examination. This is important in this day and age of increasing emphasis upon periodic health examinations and early recognition of cancer. Emphasis on the single finger technique is to be commended but one might wish the author had dropped description of the single (left) hand technique for the more rational and accurate left hand for left side of pelvis and right hand for right side of pelvis. While it is perfectly true experienced examiners have little difficulty evaluating the pelvic organs by use of left hand only, there appears to be no more reason for perpetuating this somewhat less desirable technique than there is for persistence of the old gynecological guild mark of making a straight incision with a curved scissors.

In this 3rd Edition of his book the author continues to use the term *menorrhagia* in referring to excessive menstrual flow. This reviewer prefers use of the prefix *hyper*—as being more descriptive, thus *hypermenorrhea*—in this connection. While the matter of terminology seems to be of minor significance it is important in a text for general use. It is gratifying, therefore, to find the common uterine fibroid called by its correct name—*myoma* of the uterus.

All the common gynecological conditions are discussed in an understandable manner. The general principles of treatment are likewise given but no attempt is made to detail the steps of gynecological operations.

Discussion of dysfunctional or endocrinal problems in gynecology are presented in a manner which may strike some readers as being rather brief. Actually, however, presentation of this subject is very well done. The essential known facts are given while much of the confusing, purely theoretical, highly controversial matter so likely to have been included by a less erudite, less experienced author, has been wisely left out.

Similarly, the chapter on ovarian tumors may prove a bit deceptive to the casual reader. Because of his vast experience and long interest in ovarian tumors the author is able to present this difficult subject in a comparatively simple manner giving present day knowledge without confusing the reader (as he could have done) with a mass of controversial padding.

In addition to the splendid descriptive matter which characterizes the text another outstanding feature is the fact that it is abundantly illustrated, including a large number of excellent photomicrographs which convey a more complete

AUTHOR INDEX

FEBRUARY, 1949

- Adriani, J., 31, 72
 Albert, A., 29
 Aragon, G. T., 69
 Armstrong, W. C., 47
 Arneson, A. N., 117
 Ashton, D. L., 126
 Atkinson, W. B., 100
 Austin, B. R., 46
- Bauld, W. A. G., 105
 Beerman, H., 57
 Bellas, J. E., 102
 Benson, R. C., 92
 Bernstine, J. B., 66
 Bjork, F. J., 69
 Bland, G. W., 66
 Bradbury, J. T., 42
 Brown, J. A., 103
 Brown, W. E., 42
 Butler, F. O., 66
 Buxton, C. L., 100
- Chesley, L. C., 44
 Chesner, C., 67
 Cirrerella, J. A., 67
 Cornell, E. L., 101
 Corrozzino, O. M., 57
 Costolow, W. E., 116
 Coulton, D., 97
 Cromer, J. K., 122
 Crosson, R. J., 106
 Cuyler, W. K., 113
- Davids, A. M., 143
 Davis, M. E., 87, 99, 147
 DeCosta, E. J., 110
 Diddle, A. W., 98
 Dieckmann, W. J., 69
 Diehl, W. K., 94
 Donnelly, G. C., 105
 Douglas, G. F., 150
- Elzey, N. D., 51
 Engelman, M., 90
- Farris, E. J., 96
 Felsen, J., 53
 Finn, W. F., 63
 Fluhmann, C. F., 135
- Foote, F. W., 118
 Frymire, L. J., 46
 Fugo, N. W., 99
 Fuller, H. F., 112
 Futchner, P. H., 50
- Gastineau, C. F., 29
 Goldenberg, H., 62
 Graham, R. M., 123
 Grant, K. M., 149
 Greenblatt, R. B., 27
 Gruenwald, P., 65
- Handler, S. H., 57
 Hendrickson, F. C., 142
 Hendriksen, E., 112
 Hickey, B. B., 53
 Hill, R. T., 93
 Hisaw, F. L., 107
 Holzaepfel, J. H., 64
 Hudgins, A. P., 146
 Hundley, J. M., 94
 Hunt, H. B., 124
- Ingraham, N. R., 57
- Jacobson, P., 136
 Jost, H., 40
- Kardash, T., 132
 Kegel, A. H., 154
 Kelley, A. J., 30
 Kernodle, J. R., 113
 Kriss, J. P., 50
- Lash, A. F., 144
 Leathem, J. H., 86
 Lee, T. L., 112
 L'Esperance, E. S., 113
 Li, K., 118
 Lovelady, S. B., 56
- Maas, J. M., 130
 McClintock, L., 90
 MacDonald, E. J., 115
 McElin, T. W., 56
 McGavack, T. H., 84
 McGoogan, L. S., 124
 McGraw, J., 123

Review

ANOMALIES OF THE OVARY*

REVIEW OF THE LITERATURE AND A CASE REPORT

ELI J. IGNA AND MILTON A. DARLING

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Ovarian anomalies have been encountered infrequently since Soranus, a Greek physician, reported a hernia of the ovary in 97 A.D. The literature reveals many isolated cases, but few collective reviews, or papers discussing classification, etiology, symptomatology, and therapy. A review based on the correlation of the progress made in the fields of embryology, endocrinology, and gynecology may facilitate a better understanding of the ovarian anomalies.

ANATOMY (4, 5, 7)

The ovary is attached to the posterior part of the broad ligament, and to the uterus, by the mesovarium and the ovarian ligament. The suspensory or infundibulopelvic ligament extends from the tubal extremity of the ovary to the lateral wall of the pelvis, and comprises the lateral fifth of the broad ligament that is unoccupied by the tube. It is a fan-shaped band of fibrous and muscular tissue over which the peritoneum is elevated. The ligament courses upward crossing the iliac vessels and becomes lost in the fascia and peritoneum covering the psoas major muscle. The ligament may be continuous with the lower end of the mesoappendix, or it may extend to the head of the cecum, but, most often, there is no connection between these structures.

EMBRYOLOGY (1-30)

The urogenital system arises from the mesodermal intermediate cell mass. The pronephros, which is the first structure noted, appears about the 3rd week and develops between the 7th and the 14th somites. Its tubules fuse to form the pronephric duct. The pronephros, with the exception of its duct and that portion that is destined to form the fimbriated end of the tube, disappears by the 4th week.

The mesonephric system arises at $4\frac{1}{2}$ weeks, and its tubules develop dysmetamerically (13) from the nephrogenic cord. It extends from the 6th cervical segment to the 2nd lumbar segment by the 5th week. The developing tubules bulge into the celomic cavity lateral to the dorsal mesentery producing the urogenital ridge. The persistent pronephric duct is joined by these tubules and becomes the mesonephric duct which is the inductor of mesonephric differentiation. The mesothelium is thrown into a cephalic and caudal fold by the de-

* Presented in part before the Michigan Society of Obstetricians and Gynecologists at the February 3, 1948 meeting held at The Grace Hospital, Detroit, Michigan.

- McIntyre, J. P., 47
McKay, D. G., 121
McLane, C. M., 36
McSweeney, D. J., 121
Martin, J. P., 107
Masters, W. H., 33
Mellow, J., 84
Miller, N. F., 120, 156
Moore, C. R., 85

Nieburgs, H. E., 27
Nielsen, J. M., 66
Novak, E., 127
Novak, E. R., 137

Palmer, Allan, 1
Parrett, V., 120
Patch, F. S., 141
Peightal, T. C., 131
Perry, T., 134
Platt, L. I., 122
Popence, P., 152
Potter, E., 87
Power, R. M. H., 155

Rakoff, A. E., 86
Randall, L. M., 29
Ratner, M., 140
Ravid, J. M., 109
Reddock, J. W., 59
Reis, R. A., 110
Reitman, H., 54
Riley, G. M., 120
Roman, D. A., 72
Rose, E. K., 57
Rosenfeld, S. S., 139

Rozin, S., 95
Rutledge, F., 127

Scharenberg, K., 120
Schneiderman, D., 140
Schumaker, L. B., 142
Sewall, C. W., 97
Sloan, W. R., 58
Small, C., 120
Somers, W. H., 44
Speert, H., 131
Stokes, J. H., 57
Sturgis, S. H., 123

Thomas, W. L., 113
Twombly, G. H., 90

Ulfelder, H., 119

Van Campenhout, E., 91
Vann, F. H., 44
Vogel, M., 84

Wammock, V. S., 57
Wilkins, L., 83
Winn, L., 120
Winship, T., 122
Witschi, E., 91
Wolarsky, W., 53
Wyatt, J. P., 62

Yue, H. S., 120

Zeman, F. D., 143
Zondek, B., 95

this time. Testicular characteristics are evident by the 7th week, and ovarian characteristics are evident by the 10th week. The change from an elongated structure to a short compact organ is completed by the 16th week; the ovary may rotate from the vertical to the horizontal at any time after this week. It reaches the iliac fossa during the 20th week, and the adult position in the ovarian fossa is attained after puberty.

Anomalous shapes are not unusual. The fetal ovary is characterized by a granular surface, uneven edges, and occasionally by lobulation. These, as a rule, become incorporated into the body of the ovary during puberty.

The primordial germ cells are seen in the germ sac endoderm before the 3rd week. After the 4th week, they migrate cephalad by ameboid movement, and multiply as they progress along the endodermal gut and dorsal mesentery into the epithelium of the genital ridge. The migratory period is completed after the 5th week.

The müllerian duct develops, during the 6th week, by an invaginating process of the mesothelium lateral to the mesonephros. It lies mesial to the mesonephric duct, which acts as its guide, and develops in the urogenital fold from a caudal and a cephalic anlage. The ostium always lies above the cephalic pole of the gonad. Due to its course, the müllerian duct has a cephalic longitudinal portion, a transverse portion, and a caudal longitudinal portion which are destined to form the tube, the corpus of the uterus, and the cervix and proximal portion of the vagina respectively. The uterus is indicated at 8 weeks by the beginning fusion of the müllerian ducts; however, the uterus and the tubes begin their greatest and definitive development after the 12th week. This development continues until birth.

The mesonephros and gonad arise retroperitoneally and bulge into the celom near the root of the dorsal mesentery. They carry a fold of mesothelium with them so that they are suspended by a common mesentery. The site of attachment between the 2 organs becomes constricted in the course of development between the 10th and the 16th weeks. The site and degree of constriction varies from embryo to embryo; it is the anlage of the mesovarium.

The cephalic and caudal portions of the genital ridge undergo atrophic changes. The cephalic portion develops a few solid cords of cells which grow into the mesentery common to the urogenital system. The atrophied cephalic portion of the genital ridge is continuous with the diaphragmatic ligament of the mesonephros. The joint structure is known as the diaphragmatic ligament of the ovary and becomes the suspensory ligament of the ovary. The atrophied caudal portion unites the lower pole of the ovary to that transverse portion of the urogenital ridge in which the uterus develops. This is destined to become the ovarian or proper ligament of the ovary. It is continuous with the inguinal ligament of the mesonephros which is designed to form the round ligament of the uterus.

The celomic cavities are lined with mesothelium which becomes the peritoneum with the addition of a connective tissue layer. This takes place during the 10th week at which time the intestines have become abdominal viscera.

veloping mesonephros. The cephalic fold extends from its upper pole to the diaphragm and is the diaphragmatic ligament of the mesonephros. The caudal fold extends from its lower pole to the caudal end of the celom and is the inguinal ligament of the mesonephros.

Degeneration of the mesonephros, which is dependent on the establishment of the metanephros, begins just before the 5th week and is completed, in orderly fashion, down to the first lumbar segment by the 8th week. The degenerated portion becomes the epoophoron.

Anywhere from 5 to 14 of the cephalic glomeruli and their tubules are preserved during the course of regression. This number may vary on the 2 sides of the same specimen. All the tubules, excepting the upper 3 or 4, maintain their connection to the duct for variable lengths of time, but usually they are broken before birth. The rete cords unite with those portions of the epoophoron representing regenerated glomerular capsules to form the urogenital union. This union is not necessary in the female and so it may be absent, partial, or total.

Degeneration of the lumbar area, which is divided into an upper epigenital and lower paragenital group, occurs at the 10th week. The upper is intimately associated with the development of the genital glands; the lower becomes the paroophoron. Although there are remnants present, degeneration of the mesonephric system is complete by the 16th week.

The mesonephric duct extends from the region of the mesonephros to the genital cord. In 20 per cent of the cases it forms an ampulla in the fetal cervix, and its remnants can be found in the lateral walls. Its cranial end is in the mesovarium and its caudal end is in the cervix. After the 12th week, the duct gradually regresses below the point where it parallels the developing uterus. The portion of the duct related to the paroophoron obliterates, leaving a series of closed cavities and isolated tubules. The remnant of the duct in its lower portion is known as Gartner's duct.

The metanephros, which arises from the mesonephric duct and the mesoderm caudal to the mesonephros, is seen first as the metanephric diverticulum in the area of the 4th lumbar segment at the 5th week. Its development is dependent on this diverticulum as the inductor for its differentiation. The 9th week finds it rotated so its convexity is lateral. At the 12th week, its center is at the level of the 2nd and 3rd lumbar segments. Hereafter, its movement is slower, and it embeds more deeply in the fat and connective tissue. It is opposite the first lumbar or 12th thoracic vertebra at term.

The gonad appears during the 5th week as a thickening on the ventral surface of the mesonephros. The urogenital ridge divides into a lateral mesonephric ridge and medial genital ridge. The genital ridge is covered by the mesothelium which begins to thicken and proliferate and so becomes the germinal epithelium. The gonad develops in that portion of the ridge that parallels the mesonephros. This is the middle portion and is usually in the lumbar area.

The gonad, when it first develops, is $\frac{1}{2}$ the length of the embryo. During the 6th week, it equals the mesonephros in length, and its proliferating cells invade the cephalic portion of the mesonephros. Sex changes are also manifested at

is the degeneration of the lumbar portion of the mesonephros. The intestines become abdominal viscera during the same period.

The 12th week finds the uterus and tubes beginning their definitive development; the regression of the mesonephric duct also occurs at this time.

The ovary becomes a compact organ, and the mesonephros is completely degenerated by the 16th week.

ANOMALIES (31-50)

Although the ovary develops in juxtaposition to the intestinal tract and in intimate association with the mesonephric system, it is not dependent on any of these structures for differentiation.

Due to the proximity of the embryonic ovary, adrenal, mesonephros, and the mesentery, it is not impossible to find mesonephric and adrenal structures in the ovary, and ovarian and mesonephric remnants in the mesentery. The retroperitoneal development of the urogenital system can result in the finding of ovarian and mesonephric remnants at any point along the site of the anlage. All of these have been reported with the mesenteric and retroperitoneal variety appearing as cystic degenerations.

The cause of anomalies, though unknown, has been attributed to various hereditary and environmental agents acting intrinsically, extrinsically, synergistically, or antagonistically. The response to the cause, also unknown in most instances, can be manifested in a number of ways.

The basic abnormal process is usually limited to a short period of development, leaving a part of the body in an abnormal condition. Thereafter, the affected part will develop normally but will show the effects of interference. Some ovarian anomalies show evidence of this process.

Syndromes or combinations of anomalies occur where the primary abnormality affects more than one part or when the primarily affected part influences other parts so that they become abnormal. This occurs in the development of the mesonephric duct, the metanephros, and the müllerian duct. Renal anomalies are invariably associated with genital anomalies. Experimental embryology has shown that in the absence of the mesonephric duct, there is a concomitant absence of the kidney and the müllerian duct of the same side. This is in agreement with the findings in humans.

In the light of our present day knowledge, the only workable classification of anomalies is one that is based on morphology. Such a classification of ovarian anomalies is offered, together with a review of reported cases and discussion regarding etiology, symptomatology and treatment.

Classification

I. Anomalies of Number

A. Absence (anovaria or aplasia)

1. Bilateral

a. Congenital or primary

b. Acquired or secondary

The intestinal tract, which develops between the 5th and the 12th week, is attached to the dorsal body wall by the dorsal mesentery. The omental bursa is indicated at 4 weeks at the level of the caudal end of the pronephros. The epiploic foramen, whose opening into the lesser omental sac becomes constricted with development, is evident as a broad opening at the level of the cephalic end of the genital ridge during the 6th week.

The mass of the intestines is still in the umbilical sac at the 9th week. The colon and its mesocolon, the dorsal mesentery, are on the left and act as a median septum, and so the returning intestinal loops must pass to the right. As the intestine returns, the mesocolon is displaced dorsally and to the left; the cecum and ascending colon are the last to return. As the coils increase in length, the cecum is pressed back until it reaches the dorsal abdominal wall on which it lies but to which it does not adhere. This entire process is completed during the 10th week.

The ascending and descending mesocolons grow rapidly and carry the corresponding segments of the colon far lateral in the abdomen. After the 18th week, the mesocolons become pressed against the dorsal body wall, and their flat surfaces progressively fuse mediolaterally, in varying degree, with the adjacent peritoneum. The 2 limbs of the colon become permanently anchored by the end of the 20th week. In about one-quarter of the cases, the ascending and descending colons are more or less free.

The ventral mesentery investing the blood vessels, nerves, and bile ducts becomes the duodenohepatic ligament which with the gastrohepatic ligament forms the lesser omentum. The fixation of the duodenum to the dorsal body wall results in a fold of peritoneum extending from the duodenum to the right kidney. This is the duodenorenal ligament which joins ventrally to the duodenohepatic and dorsally to the hepatorenal ligament. The latter is a fold of peritoneum extending from the liver to the ventral surface of the right kidney. The duodenohepatic, duodenorenal, and hepatorenal ligaments bound the foramen of Winslow.

SUMMARY

The urogenital system develops between the 3rd and the 16th weeks with the primordial germ cells the first structures to appear, and the mesonephroi the last to degenerate.

The mesonephric duct besides being the inductor for the differentiation of the mesonephros and the metanephros also acts as a guide to the müllerian duct. The degeneration of the mesonephros is dependent on the establishment of the metanephros.

The metanephros, gonad, and the intestine begin to develop during the 5th week. The gonad manifests sex changes, and the müllerian duct appears during the 6th week. The uterus begins to form during the 8th week. The suspensory ligament, the ovarian ligament, the broad ligament, and the round ligament of the uterus are all apparent by the 9th week.

Concomitant with the evidence of ovarian characteristics during the 10th week

equals its normal counterpart in function. This condition has been attributed to a third anlage, duplication of gonadal and tubal anlage, complete longitudinal or transverse splitting of the gonad, and failure of degeneration of the genital ridge. In 12 reported cases, the functional supernumerary ovary was found in the abdominal or pelvic cavity, and it was associated equally with a third tube or an ovarian ligament. A functioning third ovary not associated with a third tube or an ovarian ligament has been reported in 6 cases. E. S. Hoffman (64) encountered a third ovary, not reported previously, in a patient who had had a right salpingo-oophorectomy and left salpingectomy followed in a few years by a supracervical hysterectomy and left oophorectomy. The symptoms were severe left lower quadrant pain and associated vaginal spotting at 1 to 3 month intervals. The ovary was at the pelvic brim and retroperitoneally situated. Biopsy revealed a corpus luteum of the ovary. Postoperative deep ray therapy alleviated all symptoms.

Retroperitoneal or intraligamentous non-functioning third ovary or ovarian remnant was reported in more than 50 cases. There was no connection to the normal ovary, and no associated third tube or ovarian ligament was found in any of these cases.

In the majority of cases, cystic degeneration of the ovary may occur with the resultant symptoms of ovarian or retroperitoneal cyst. The diagnosis, usually evident at the time of surgery, may necessitate a biopsy for verification.

Periodic bleeding and pain are the symptoms in the cases where the normally situated ovaries have been removed. Hormone studies and curettage may aid in the diagnosis which is usually made at the operating table.

The accessory ovary, which may be non-functioning, is attached to the normally situated ovary by a pedicle that varies in length and which consists of ovarian stroma and/or connective tissue. This structure, which may be multiple, can be found anywhere along the site of the anlage, at the hilus of the ovary, in the ovarian ligament, in the mesovarium, in the broad ligament, or it may be attached to the peritoneum, mesentery, or the intestine. This group also comprises the lobulated ovary, the bipartite, the partita, the disjuncta, the succenturiata, and the multiple excrescence varieties of ovary. In the multiple excrescence type, 3 per cent of the cases show the presence of ovarian stroma in the excrescences. Keller (65) gives the incidence of accessory ovary as 1 in 7800 gynecological cases or 1 in 2700 laparotomies. The incidence of tumors or cystic degeneration in this group has been reported to range from 69 to 100 per cent of which but 6 to 7 per cent were malignant (68).

The accessory ovary may be the result of incomplete and/or spotty or segmental degeneration of the genital ridge, partial splitting of the gonad, or failure of the ovary to incorporate the excrescences. It is usually an incidental finding at the time of surgery or autopsy.

ANOMALIES OF SIZE (80-87)

The elongated or giant ovary, which is long, hard and white, may be the result of failure of the ovary to become a compact organ, or it may be due to constitutional disease. There have been 124 cases reported with a few being bilateral.

- 2. Unilateral
 - a. Congenital
 - b. Acquired
- B. Supernumerary
 - 1. Functional
 - 2. Non-functional
- C. Accessory
- II. Anomalies of Size
 - A. Elongated or giant
 - B. Rudimentary
 - C. Ovotestis
- III. Anomalies of Position
 - A. Hernia
 - B. Descent
 - 1. Bilateral
 - 2. Unilateral
 - C. Loose bodies in abdominal or pelvic cavity
- IV. Mixed Anomalies
 - A. With other ovarian anomalies
 - B. With other urogenital anomalies
 - C. With other intestinal anomalies
 - D. With external anomalies

ANOMALIES OF NUMBER (51-79; 110)

Primary bilateral absence of the ovary occurs as a result of defective germ plasm and is associated with non-viable monstrosities. The condition has never been reported in an adult.

Secondary bilateral absence, due to destruction of the ovary by trauma and infection, has been reported in a few cases. The symptoms are amenorrhea and hypogonadism. The diagnosis is dependent on a high follicle stimulating hormone level and a low 17 ketosteroid level.

Congenital unilateral absence of the ovary is due to failure of the anlage to develop. It is usually associated with anomalies of the müllerian duct and the metanephric system. The incidence, based on 10,000 autopsies, is 0.05 per cent. The majority of the 33 reported cases were associated with other developmental defects, and in all the reported cases, the diagnosis was made at the time of surgery or autopsy and usually was an incidental finding.

Torsion of the tube and ovary with resultant degeneration is the etiologic factor in acquired unilateral absence of the ovary. The differentiating criterion of this group is the persistent tubal stump which was observed in all the reported cases. The symptoms simulate those of torsion of the pedicle of an ovarian cyst or of a hydrosalpinx. The diagnosis is dependent on the history of such symptoms; however, most often it is diagnosed at the time of surgery.

A supernumerary ovary is not attached to the normally situated ovary, and it may have its own ovarian ligament or an associated third tube. The third ovary can have an abdominal, retroperitoneal, or intraligamentous location, and it

distinction to the incidence of associated genital defect with renal anomaly which ranges from 10 to 45 per cent.

The anomalies of position may be associated with some intestinal anomaly. The defects reported are failure of rotation, faulty position of the cecum and ascending colon, and failure of complete fusion of the mesocolon.

Congenital faults of the ovary are likely to be associated with extrinsic general genetic deformities of varying degrees. The bilateral congenital absence of the ovary, which is associated with non-viable monstrosities, is the best example of this process.

CASE REPORT

The patient, E. W., a 34 year old nurse was seen in consultation on January 23, 1945. She had been admitted to the hospital on December 14, 1944, complaining of right upper quadrant pain, nausea and vomiting, and increasing dysmenorrhea. The pain was sharp, intermittent, and radiated to the back. These symptoms were premenstrual in onset and were alleviated by menstruation. A complete blood count, urinalysis, and fasting blood sugar were within the normal range. The patient was discharged following symptomatic therapy.

She was readmitted on January 10, 1945 with an increased severity of the symptoms. Further study revealed a mild cholecystitis, right upper quadrant and costovertebral angle tenderness. Blood counts done on the 10th and the 11th showed a leucocytosis of 16,600 of which 70 per cent were polymorphonuclear cells, and 13,200 of which 80 per cent were polymorphonuclear cells. The gastroenterologist considered this a probable anatomic dyskinesia with symptoms referable to the gallbladder and colon.

Menarche occurred at 11 years of age and was characterized by a 28 day cycle and a 4 day moderate flow. There was no dysmenorrhea prior to the present illness.

At an early age her right middle finger was amputated because of malformation. In 1937 her appendix was removed.

At the time of examination, the patient was free of pain. An asymmetry of the face, absence of the right middle finger, an apparent fusion of 2 of her right toes, and a healed right rectus incision were noted.

Pelvicly, a small fixed uterus was palpated. A tentative diagnosis of endometriosis was made with the recommendation that examination under anesthesia be done with permission to perform a laparotomy if findings so indicated.

On January 27, 1945, under anesthesia, there was no apparent uterine or left adnexal pathology. The right ovary could not be palpated. An ill-defined mass, thought to be bowel attached to the posterior fundal wall, was palpated in the right upper portion of the pelvis. In the presence of these findings, a laparotomy was deemed advisable.

At surgery, no gross pathology of the uterus or left adnexal structures was seen. The right fallopian tube and the ovarian ligament extended to the iliac fossa where the elongated and narrow ovary was found lying posterolateral to the mobile cecum. A smooth, lobulated, cystic mass (8 x 5 x 3 cm.) whose sur-

Microscopically, they are characterized by an increased cortex and follicles with multiple ova. The symptoms may be amenorrhea, menstrual irregularity, abnormal bleeding at puberty, and occasionally moderate masculinity. The clinical diagnosis is more than difficult and the therapy is unknown.

The rudimentary ovary, which contains ovarian stroma but has no follicles, results from the failure of the follicular epithelium to develop. It is associated with infantilism, and clinically there is amenorrhea, hypogenitalism, the other endocrine glands are normal, and the hair distribution may be normal. The diagnosis, as in the case of absence of the ovaries, is dependent on a high follicle stimulating hormone level and a low 17 keto-steroid level. There have been 50 cases reported.

An ovotestis is a gonad which has not progressed beyond the fetal period. It contains varying amounts of ovarian and testicular architecture, and is found primarily in hernias.

ANOMALIES OF POSITION (88-102)

Inguinal hernia of the ovary, which represents 95 % of ovarian herniations, is the most common anomaly of position. If the tube accompanies the ovary, the term inguinal ectopia is applicable. Its cause is unknown, and it is found primarily in infants.

Descent of the ovary, be it apparent or real, is due partly to the degeneration of the cephalic portion of the genital ridge and largely to the upward growth of the abdomen and pelvis and to the straightening of the back. Inhibition anywhere along the site of the anlage may result in varying degrees of failure to descend abdominally or retroperitoneally.

Bilateral failure to descend has been reported in 2 cases. In 1, both ovaries were elongated and at the level of the 3rd and 4th lumbar vertebrae; from their lower poles, a ligamentous fold led into the immediate retroperitoneal area. In the other, there was a dermoid cyst of the right ovary and a papillary cystadenoma of the left ovary.

There have been 10 cases of unilateral failure to descend reported. Seven of the cases were right-sided and 6 of them were operated upon with the diagnosis of appendicitis. One was a pyosalpinx and ovarian abscess in the false pelvis, and another was found at autopsy following a neonatal death. Two cases were unobtainable for review.

Two cases of intraligamentous ovary and tube and a case of a loose body, thought to be an amputated ovary, in the cul-de-sac have been reported.

MIXED ANOMALIES (103-108)

Any type of ovarian anomaly may occur independently, or may be associated with any or all of the other types. This is particularly true of the anomalies of number and position, with the anomalies of size being involved occasionally.

The anomalies associated with other urogenital anomalies are those showing absence of the ovary, failure of descent, and the rudimentary ovary. The incidence of associated defect of the ovary and kidney is 1 per cent and less in contra-

distinction to the incidence of associated genital defect with renal anomaly which ranges from 10 to 45 per cent.

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FIG. 1. SPECIMEN SHOWING THE OVARY, PEDICLES, AND CYST OF THE ACCESSORY OVARY

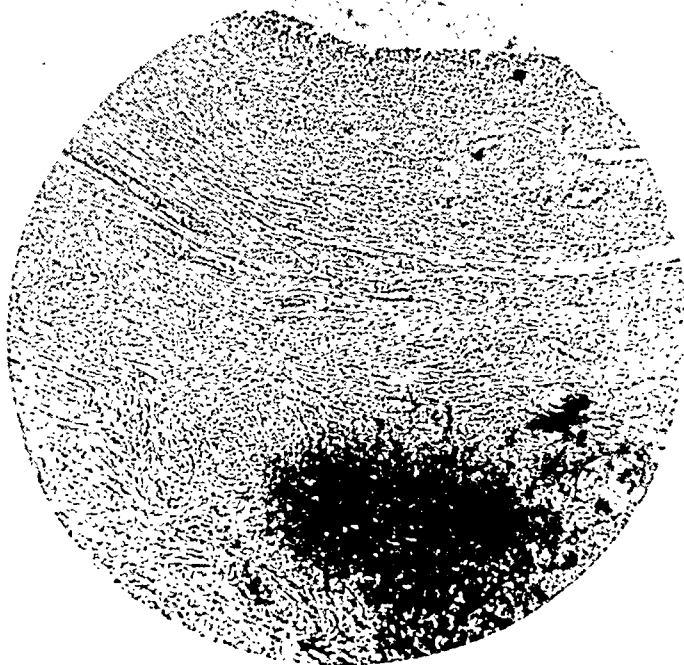


FIG. 2. SECTION TAKEN THROUGH AREA OF CYST PROXIMAL TO THE PEDICLE LEADING FROM THE OVARY ($\times 125$)



FIG. 3. LINING OF CYST (X450)

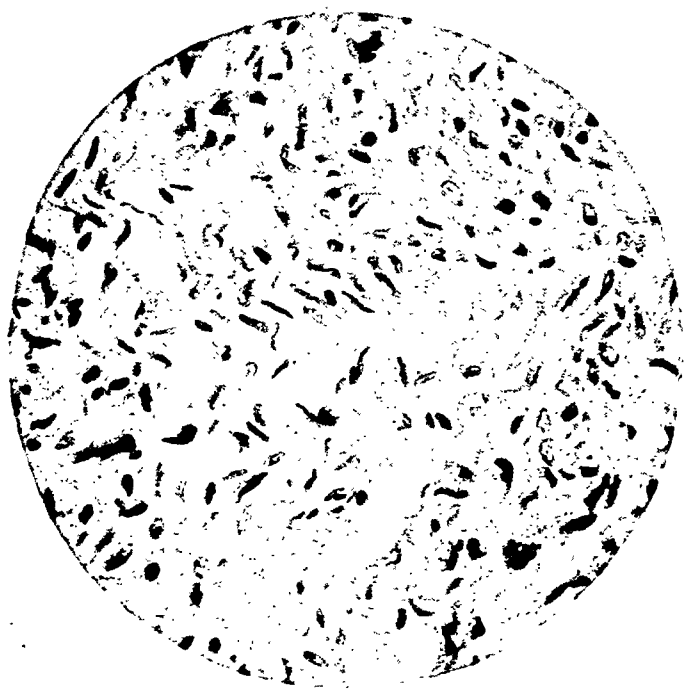


FIG. 4. PEDICLE TO THE ACCESSORY OVARY (X450)

face showed areas of purplish discoloration was found lying over the kidney. There were 2 multiply twisted pedicles extending from either pole of the cyst. The caudal pedicle was thick and connected to the ovary. The cephalic one was thin and extended to the foramen of Winslow where it fused and blended with the peritoneum and ligaments forming the foramen. The ovary, cyst, and pedicles were removed. (Fig. 1)

The pathologist reported a unilocular cyst containing a thick colorless fluid. The cyst wall varied in thickness and consisted of fibrous connective tissue and ovarian stroma. (Fig. 2) The lining was characterized by areas of flat cells, cuboidal cells, and broad flattened papillary projections. (Fig. 3) The pedicles were composed of ovarian stroma and connective tissue. (Fig. 4) The cyst wall and pedicles showed areas of hemorrhage. The pathological diagnosis was paroophoron cystoma of the ovary with strangulation.

The report of the findings at the time of the appendectomy revealed absence of pathology of the uterus and left adnexal structures (109). The right tube was found leading laterally out of the pelvis to an elongated and narrow right ovary lying in front of the right kidney. The impression was that it was attached to the root of the mesentery by a thick short pedicle.

The patient's course in the hospital was uneventful. Follow-up examinations over a 2-year period were negative.

DISCUSSION

This case represents an anomaly of number, anomaly of position, and a mixed anomaly because it is an accessory ovary attached by a pedicle of ovarian tissue to the normal ovary which was lying in the iliac fossa. Associated are the external anomalies of malformed finger, fused toes, and asymmetry of the face.

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Obstetrics

PHYSIOLOGY OF PREGNANCY, LABOR AND PUERPERIUM

THE PERMEABILITY OF THE HUMAN PLACENTA TO WATER AND THE SUPPLY OF WATER TO THE HUMAN FETUS AS DETERMINED WITH DEUTERIUM OXIDE

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Am. J. Obst. & Gynec. 56: 861-868, November, 1948

In a previous paper, findings were presented on the permeability of the human placenta to sodium as determined with the radioactive isotope and the theory of the tracer technic in investigations of this kind was discussed. The authors' present concern is with the permeability of the human placenta to water, using deuterium oxide (heavy water) as the tracer substance. As in other studies from their laboratory, the authors analyze their data from the viewpoint of the following questions: (1) Does the permeability of the human placenta to water change with the period of gestation? (2) Is the permeability of the human placenta to water approximately like that of another member of the hemochorial group, the guinea pig, as is true for sodium? (3) What is the relative permeability of the human placenta to water and sodium? (4) Does the human fetus, like the fetus of the guinea pig, receive quantities of water greatly in excess of the amount incorporated in growth?

Ninety-five per cent deuterium oxide (D_2O) made isotonic with sodium chloride was injected into 7 patients whose pregnancies were being terminated by the abdominal route at various periods of gestation and for various medical reasons. The quantity of water transferred to the fetus per hour at various fetal ages was found to be 3.6 liters of water per hour at the peak of the curve, which is at about the 35th week of gestation. Closely approximating the results with sodium there is about a 5-fold increase in permeability of the placenta to heavy water from the 14th week of pregnancy, the earliest case in the series, to the peak which occurs at about the 35th week. This peak in permeability at the 35th week is followed by a sharp decline to term.

The ratio of the quantity of a substance supplied to the fetus from the maternal plasma to the amount of that substance retained by the fetus in its growth has been called the safety factor for that substance. The value of the safety factor for water varies from 700 at a fetal age of 14 weeks to the extraordinarily high value of 3800 at 30 weeks. This means that of 3800 parts of water delivered to

the fetal circulation at 30 weeks, only one part is retained by the fetus in its growth and 3799 parts are returned to the maternal circulation.

The increase in the permeability of the placenta to sodium as gestation proceeds has been correlated with morphological changes in the placenta as it ages (Am. J. Obst. & Gynec. 55: 469, 1948). Variations in the permeability of water are similar to sodium and again it appears that thinning of the walls of the villi together with increase in area of placental exchange due to branching of the villi are fundamental factors underlying the increase in permeability. The terminal sharp decrease in placental permeability is probably due in considerable measure to the deposition of fibrin over the surface of the villus.

(See editorial note following next abstract.—Ed.)

THE RATE OF RENEWAL IN WOMAN OF THE WATER AND SODIUM OF THE AMNIOTIC FLUID AS DETERMINED BY TRACER TECHNIQUES

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Am. J. Obst. & Gynec. 56: 1156-1159, (December) 1948

Although the injection of dyes has demonstrated that exchange of an artificial constituent of the amniotic fluid may take place with the maternal plasma, (Boucek and Renton, Surg., Gynec. & Obst. 54: 906, 1932; Albano, Zentralbl. f. Gynäk. 58: 975, 1934) it was impossible to obtain a reliable and precise picture of the dynamics of the naturally occurring constituents of the fluid until radioactive and stable isotopes became available for experimental purposes. Measurements made with the isotope technique in the guinea pig showed that the water of the fluid at all stages of gestation is completely replaced at the surprisingly rapid rate of about once an hour, whereas the rate of replacement of the sodium is about 50 times slower (Am. J. Physiol. 136: 757, 1942). The authors have now measured water and sodium transfer to the human amniotic fluid using deuterium oxide (heavy water) and radioactive sodium (Na^{24}) as the tracer substances. The observations with water were made on 5 women, and with sodium on 20 women, on whom hysterotomies were performed for medical reasons.

On the average, 34.5 per cent of the water of amniotic fluid is replaced per hour by water from the maternal plasma. This means that the average rate of renewal of the water of the amniotic fluid is once every 2.9 hours. The sodium of

the fluid is renewed at the average rate of 6.9 per cent of that present per hour; i.e., the sodium of the fluid is turned over once every 14.5 hours. There is considerable variation, apparently unrelated to gestational age, among the observed rates both for water and sodium.

The rate at which water is transferred to the amniotic fluid is considerably greater than that for sodium. Whereas the amount of water which flows into and out of the amniotic sac in 3 hours is approximately equal to the volume of the amniotic fluid, only about $\frac{1}{5}$ of the total sodium is replaced in the same interval. This means that water is renewed about 5 times as rapidly as sodium. When a comparison of the rates of transfer of water and sodium across the placenta in the guinea pig was made, a similar difference was noted (*Am. J. Physiol.* 136:750, 1942). Evidence was given which could explain the observations completely on the basis of greater permeability of the placental membrane to water than to sodium. The same explanation, applied to whatever membranes are involved, may hold for the difference in transfer rates of water and sodium from the maternal circulation to the amniotic fluid.

It will be apparent from the large difference in rate of transfer of water and sodium to the amniotic fluid that it is impossible to make reliable deductions about the rate of exchange of the normal constituents of the fluid from observations on foreign substances like dyes.

The main source of the amniotic fluid has been thought by some investigators to be fetal urine. The present experiments shed no light as to the principal site at which the exchanges of water and sodium between the maternal blood and amniotic fluid takes place. It was pointed out in studies on the guinea pig (*Am. J. Physiol.* 136:757, 1942) that in the earlier stages of pregnancy a volume of water equal to that of the fetus flows in and out of the amniotic sac in an hour, and that it would seem questionable that the fetal urine could alone account for this relatively large volume of fluid. The results in women substantiate this view. At the 10th week of gestation, for example, 40 cc. of amniotic fluid may be associated with a fetus weighing less than 20 Gm. (Needham, J.: *Chemical Embryology*, Cambridge University Press, 1931) and the water of this fluid will be completely replaced in about 3 hours. At term a fetus weighing 3.4 kg. is surrounded by approximately 1000 cc. of amniotic fluid which is exchanging water at the rate of approximately 350 cc. per hour. This astonishingly rapid rate of replacement of the water of the human amniotic fluid, like that of the guinea pig, is at variance with the concept that the amniotic fluid is a relatively stagnant body fluid.

(This group of authors, headed by Flexner of the Department of Embryology, Carnegie Institution, Baltimore, have provided an entirely new concept of the placental barrier. By the use of radioactive isotopes they have been able to study for the first time the behavior of naturally occurring constituents of the blood and amniotic fluid in respect to placental transmission in contradistinction to the behavior of dyes and other extraneous substances. Possibly the most astonishing feature of placental transfer which their studies have demonstrated, is the huge volume of materials which this organ is constantly shifting back and forth across the placenta. For instance, the authors' statement that the amniotic fluid is exchanging water at the rate of 350 cc. an hour is scarcely credible but must be accepted on the basis of this sound work. The picture becomes all the more amazing when it is recalled

that while the molecules in this 350 cc. of water are migrating in one direction, an approximately equal number of molecules of water are passing in the other.

There used to be much discussion as to whether the process of placental transfer is one of simple diffusion or one of selective activity. Although both mechanisms are probably concerned, evidence such as the above would seem to give selective activity a predominant role because it is difficult to conceive how simple diffusion could bring about such an extremely active state of flux.—Ed.)

ERYTHROCYTE SEDIMENTATION VELOCITY (B.S.R.) IN NORMAL PREGNANCY

E. OBERMER

J. Obst. & Gynaec. Brit. Emp., 55: 464-469 (Aug.) 1948

That the velocity of erythrocyte sedimentation is increased during normal pregnancy has been known since 1921; however, there has been doubt as to when this increase occurs during the course of gestation. Due to the variety of tests in use, there has also been a wide range of change noted in the B.S.R. determinations. The author has devised a simple technique of determining the sedimentation rate based on the original method of Balachowsky. A 10.4 cm. capillary tube, 0.2 cm. in diameter, is filled with oxalate and then emptied so that 0.4 cm. of oxalate remains in the tube. A deep prick is made in the finger and the tube is filled half full by capillary action on the drop of blood obtained. The tube is then inverted and the filling completed from the other end of the tube. It is placed upright and readings are taken at 15 minutes, 30 minutes and one hour with a ruler graduated in centimeters and millimeters. Normal limits with this method are: 15 minutes, up to 0.4 cm.; 30 minutes, up to 1.0 cm.; and 60 minutes, up to 2.5 cm. Corrections for the red blood cell count need to be made only if the count is below 4 million or over $5\frac{1}{2}$ million. In such instances, the reading should be multiplied by the following factor:

RBC in millions

5

The author presents the sedimentation velocity figures from a series of one abnormal and 88 normal pregnancies in tabular and graphic form. Two hundred and eighty-three determinations were carried out on these women and the rates were averaged for each 4-weekly period during pregnancy. It was demonstrated that in the majority of normal pregnant women, sedimentation velocity increases slightly as early as the fifth to sixth week. From the eighth week onward, there is a regular increase in the velocity up to a maximum at the fortieth week. The average rates at the fortieth week by this method were: 15 minutes, 2.7 cm.; 30 minutes, 4.2 cm.; and one hour, 5.0 cm. After labor the velocity falls swiftly, in 4 weeks to almost normal limits, and by 8 weeks to the normal range for the nonpregnant state. There was very little scatter from the mean of this series;

however, there was a small percentage of cases which manifested unusually slow or rapid rates. One case remained within normal limits until the twenty-fifth week and at term was still below average. A second case, however, was as high at the eighth week as the average case at the twelfth week, and remained above average throughout the pregnancy. The mechanism of these variations is as yet unexplained. In a third case in which intrauterine death occurred at about the thirty-fourth week, a steep fall occurred at the thirty-seventh week (practically to the normal level for the nonpregnant state). There was no clinical evidence for suspecting any abnormality in the pregnancy.

(Contacts with a good many internists have led me to believe that they are often not cognizant of the increased sedimentation rate in normal pregnancy and occasionally draw incorrect conclusions from this test in cases of rheumatic heart disease and tuberculosis complicated by gestation. As Obermer points out, the sedimentation velocity increases very early in pregnancy, that is around the fifth or sixth week. In this connection it may be recalled that Fahreus, who devised the blood sedimentation test, first recommended it as a test for early pregnancy. It soon became evident, however, that all kinds and degrees of infection increase sedimentation velocity and hence, because of lack of specificity, the test was abandoned as a diagnostic aid in pregnancy. It nevertheless becomes useful now and then to bear in mind the fact that the blood sedimentation rate does increase very early in pregnancy, becomes more rapid as gestation advances and during the early puerperium attains an extremely swift rate.—Ed.)

PATHOLOGY OF PREGNANCY

A DIETARY AND CLINICAL SURVEY OF PREGNANT WOMEN WITH PARTICULAR REFERENCE TO TOXAEMIA OF PREGNANCY

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J. Hygiene, 46: 198-216 (July) 1948

The chief purpose of this study was to investigate the dietary habits and food intake of a representative group of pregnant women in the period immediately following the war, and to ascertain how far this food intake met the various requirements recommended in pregnancy. The second purpose was to elicit any information from clinical investigation and history of the subject and correlate any clinical findings with dietary intake. A survey was made of the diets of 111 normal pregnant women during 1947 by the individual method (Widdowson, 1936). The subjects were primiparae who represented the better type of women in the poor and middle-class sections of the community. Four patients were in the first 3 months of pregnancy, 96 were between 3 and 6 months and 11 were between 6 months and term.

The survey estimated the total food intake over a period of one week; blood samples were also taken for biochemical and hematological examinations. Full records were kept of the money spent on food, husband's occupation, clinical history during pregnancy and the neonatal period. The health and clinical history of the infant resulting from the pregnancy were also recorded during the neonatal period.

Each subject was given a spring-balance on which to weigh all food taken over a period of one week and a book in which to record details of each meal. The weighing and recording were supervised by a health visitor. The chemical composition of the diet was analyzed from food tables and figures from numerous sources in the literature, and estimations were made of calories, protein, animal proteins, fat, carbohydrates, calcium iron, vitamins A, D, C, and B₁, riboflavin and nicotinic acid.

The author describes the results of the study first in terms of articles of diet. Comparisons are made with mean values for these foodstuffs found by McCance in 1938 in 120 pregnant women of low income.

The mean intake of bread was 56 oz. per week, compared with the 77 oz. per week allowed under the rationing system; the mean intake in this group was 17 per cent greater than in McCance's group. Bread is most important as a provider of vitamin B₁, iron, nicotinic acid, calories, riboflavin and calcium.

This group was taking 90 per cent more milk on the average than McCance's group, their mean intake being 123 oz. per week while the ration allowed was 190

oz. per week. Only 21 per cent were taking more than one pint per day, and at least 80 per cent were not taking their full ration. The total intake of chemical constituents provided by milk in this survey was: 50 per cent of the calcium, 42 per cent of the riboflavin, 33 per cent of the animal protein and 17 per cent of the vitamin B₁.

The mean intake of margarine (fortified) was 8 oz. per week, a drop of 20 per cent from McCance's study, and compared with the 6 oz. per week ration allowance. In this survey butter and margarine provided only 2 per cent of the vitamin A and 6 per cent of the vitamin D, the bulk of these vitamins being supplied by vitamin supplements.

The mean intake of potatoes was 44 oz. per week, or 47 per cent more than McCance's group consumed. Potatoes provided 16 per cent of the total ascorbic acid, 12 per cent of the vitamin B₁, 12.5 per cent of nicotinic acid and 10 per cent of calories.

In assaying the intake of vegetables, particular attention was paid to the method of cooking. The mean intake was 26 oz. per week, or 18 per cent more than McCance's pre-war group.

The total meat intake includes all meat, rabbit, chicken, bacon, pork, ham and offals, most important sources of animal protein and nicotinic acid. Liver is the commonest offal and the richest source of vitamin A. The mean intake of 20 oz. per week was 5 per cent lower than in McCance's group.

The mean intake of fish was 10 oz. per week, or 43 per cent higher than in the pre-war group.

As regards nutrient principles of the diet, the mean intake of 2400 calories agrees fairly well with the intake of 2500 calories in the National Research Council (U. S. A.) standard for pregnant women and is a little higher than the 2360 calories taken by McCance's group. Generally speaking, the greater the caloric intake, the more likely it is to contain adequate vitamins and mineral salts.

In recent years there has been considerable evidence that a low protein intake may be associated with toxemia. Of particular importance in pregnancy is the relationship of methionine deficiency to liver damage and tryptophan in replacing nicotinic acid. The mean intake of 1.5 g. protein per kg. body weight agrees well with the recommended figure of the N.R.C.; only one subject was receiving less than 1 g. per kg. body weight and only one subject had a plasma protein level lower than 5.5 g./100 cc. The protein also contained a satisfactory proportion of animal protein, the mean intake being 50 g. per day. McCance's figures for total protein and animal protein were 1.2 and 43, respectively. The 17 cases of toxemia which occurred bore no relationship to the intake of protein.

The importance of milk as a provider of calcium during pregnancy is shown by the fact that 50 per cent of the calcium intake in this group came from milk. The mean intake was 1.2 g., compared with 0.7 g. in the pre-war group. By comparison with standard B (N.R.C. standard for sedentary women) the diets as a whole were adequately supplied with calcium, but they were poor compared with standard A (N.R.C. standard for pregnant women).

The mean intake of iron without supplements was 14.0 mg. per day, compared

with 12.0 mg. per day in McCance's group. Even without supplements the iron content was good, 44 per cent reaching standard A. Dietary iron was supplied by bread 30 per cent, meat 30 per cent and vegetables 30 per cent.

Eighty-four per cent of this group were taking vitamin A supplements, equivalent to a daily intake of 4000 units of preformed vitamin A, so that all subjects had sufficient intake of vitamin A; 86.5 per cent reached standard A. The dependence upon vitamin supplements and liver for vitamin A is shown by the fact that if these 2 sources are eliminated only 48 per cent were receiving sufficient vitamin A for standard B.

Vitamin supplements provided 800 units of vitamin D per day and were taken regularly by 84 per cent of the group. One very obvious point emerges, namely, that 95 per cent of the women would have had an intake less than 400 units per day if they had relied on natural sources of vitamin D.

The mean intake of vitamin B₁ was 1.25 mg., compared with 1.0 mg. in McCance's group. Only 1 per cent reached standard A and 23.4 per cent were below standard B. Bread supplies on the average 37 per cent of the vitamin B₁. The 17 cases of toxemia did not appear to bear a constant relationship to the intake of vitamin B₁.

The mean intake of riboflavin was 1.7 mg. Thirty per cent were below standard B and 3 per cent reached standard A.

The mean intake of 10 mg. per day of nicotinic acid was less than 11 mg. recommended on standard B. Seventy-four per cent failed to reach standard B and none reached standard A. Compared with all other nutrients, the diets were worse in nicotinic acid content than in any other due to the shortage of meat and offals in the present-day diet. In the group of 17 patients who developed toxemia, the mean nicotinic acid intake was lower than that in the normal group. The difference was statistically significant. The diet of one patient who had the severest degree of toxemia (eclampsia) was particularly interesting in that it showed a high vitamin B₁ intake and a low nicotinic acid content. The possibility arises that deficiency of nicotinic acid or some other factor of the B₂ complex may be a predisposing factor in toxemia of pregnancy.

The mean intake of vitamin C was 81 mg. per day, compared with 100 mg. required on standard A and 70 mg. on standard B. The 50 mg. a day recommended by the League of Nations is probably adequate. In this group, 25 per cent reached standard A, 40 per cent failed to reach standard B, and 18 per cent failed to reach 50 mg. per day.

The clinical results of this study are presented. A diagnosis of toxemia was made if the blood pressure exceeded 140/90, where it had previously been normal or where albuminuria occurred.

There were 2 miscarriages and 4 stillbirths. While the number of each is too small for conclusions, it is noted that there were definite dietetic deficiencies in 4 of the 6 cases.

Of the 17 toxemia cases, many were on quite good diets; only one did not take the vitamin supplements daily. Six had rather poor milk intakes, but the rest were very satisfactory in this respect. The great majority had low intakes of

bread and meat resulting in poor intakes of vitamin B₁ and nicotinic acid. However, the nicotinic acid intake was universally low, while 2 of the diets had quite high intakes of vitamin B₁. The nicotinic acid intake (mean) of the toxemia patients was 8.3 mg.; that of the 94 non-toxemic patients was 10.3 mg., the difference being statistically significant. The minimum daily requirements in a normal adult are given as 10 mg. by the United States Food and Drug administration.

Various investigators have found an association between toxemia of pregnancy and pellagra, vitamin B deficiency and undernourishment. It is hoped that the findings in the present study of a close relationship between a deficiency of vitamin B₂ complex and toxemia will stimulate further work to determine if these vitamins have any effect in the prevention of toxemia of pregnancy.

From the present study, the main cause of defective nutrition appears to be ignorance and not lack of money; this is an additional reason for promotion of an intensive nutritional education program. The appointment of dieticians to antenatal clinics is stressed as an important step in this respect.

The use and abuse of recommended allowances in pregnancy is discussed and the following diet is suggested as a reasonable practical allowance for pregnant women: calories, 2500; protein, 1.5 g. per kg. body weight; calcium, 1.5 g.; iron, 15 mg.; vitamin A, 3500 units (pre-formed); vitamin D, 800 units; vitamin B₁, 1.5 mg.; riboflavin, 2.0 mg.; nicotinic acid, 14 mg.; and vitamin C, 50 mg. 3 figures.

(The great decrease in the incidence of eclampsia in most areas of the United States during recent years is difficult to explain on any convincing basis, but there are many who suspect that a dietary factor is involved. In this exhaustive and painstaking study, the suggestion is made that nicotinic acid deficiency, or at least some deficiency of the B complex, may be responsible. Some plausibility is lent to this suspicion by the fact that the geographic distribution of eclampsia in this country shows a striking relationship to the distribution of the vitamin B complex deficiencies. This has been stressed especially by A. C. Siddall in two articles: *Am. J. Obst. & Gynec.* 35: 1662, 1938 and *Idem* 39: 818, 1940. In the latter of these articles Siddall presents two maps which document very clearly the fact that eclampsia is much more prevalent in the southeastern quadrant of the United States than elsewhere. It is a significant fact that in this same quadrant occurs almost all the pellagra in this country. Indeed, it has been estimated that some 200,000 persons are afflicted with pellagra in this area. The highest incidence, Siddall points out, is among adult married women which suggests a relationship between pellagra and pregnancy and lactation. No other vitamin deficiency is so localized in the southeastern states. Siddall adduces other evidence to show that in countries where pellagra is rare, eclampsia is also uncommon.

Studies of the seasonal incidence of eclampsia would seem to indicate that the disease shows a steady increase in the number of cases beginning in February and reaching a maximum in April. This is the time of year of course when fresh foods are least available, when food prices reach their highest and when malnutrition in general increases. The importance of this seasonal malnutrition factor is shown by the circumstance that most cases of pellagra likewise develop in the late winter and spring.

All this constitutes suggestive evidence that vitamin B complex deficiency may have something to do with the etiology of eclampsia. It must be regarded as suggestive, however, and no more. Further studies along this line, therefore, will be awaited with interest.

—Ed.)

DOES ECLAMPTOGENIC TOXEMIA CAUSE CHRONIC HYPERTENSION?

L. C. CHESLEY

Bull. Margaret Hague Mat. Hosp., 1: 81-84 (Sept.) 1948

The writer believes that prolonged toxemia probably does cause chronic hypertension. A correspondent has written to the effect that so eminent an authority as Dieckmann does not think that preeclampsia causes chronic hypertension.

The majority of investigators have found a relationship between the duration of toxemia diagnosed as preeclampsia and the incidence of hypertension as found at follow-up. However, not all authorities are agreed that preeclampsia does *cause* the persistent hypertension. Dieckmann (Am. J. Obst. & Gynec., 36: 798, 1938) does not believe that the hypertension of preeclampsia exists long enough to cause permanent vascular damage. If hypertension be found at follow-up examination, his final diagnosis is "vascular renal disease," whatever may have been the clinical picture in pregnancy. If the blood pressure be normal at this time, the toxemia is classified as preeclampsia. Obviously, preeclampsia diagnosed in this manner is not followed by persistent hypertension. In discussing Dieckmann's paper, Eastman postulated a patient who, in the last month of pregnancy, develops acute hypertension, proteinuria and edema. If all these signs have disappeared by 6 weeks postpartum, the case is called preeclampsia. If the hypertension persists, Dieckmann would classify the toxemia as essential hypertension. Eastman concedes that she may have essential hypertension at 6 weeks postpartum, but points out that the pertinent question is "what did she have during the last month of pregnancy?" He feels, as the author does, that she had preeclampsia resulting in chronic hypertension.

Dexter and Weiss state that in the human 3 weeks of hypertension in the pulmonary circuit is long enough to produce detectable vascular damage. It might be argued further that preeclampsia is not only hypertension, but it is also a disease in which some agent directly and generally causes morbid changes in the vascular tree.

When the incidence of posttoxemic hypertension is plotted against the duration of the toxemia (diagnosed as preeclampsia during pregnancy), a regularly rising curve is obtained. With 3 weeks of toxemia, the incidence of residual hypertension jumps to about 40 per cent; with 4 weeks, about 60 per cent are left with hypertension, and with more than 4 weeks, about 67 per cent.

There are 2 possible explanations for this curve relating the incidence of posttoxemic hypertension to the duration of toxemia. First, longer duration of toxemia causes progressive vascular change which is reflected in the hypertension. Second, with longer duration of toxemia, a larger and larger proportion of the patients are hitherto latent hypertensives, and a progressively small proportion are true preeclamptics. The validity of the latter interpretation may be tested by comparing the incidences of residual hypertension in 2 groups of posttoxemic pa-

tients: those whose pregnancies were interrupted, and those allowed to go on to spontaneous labor. If the second interpretation be true, then the form of the curve should be altered and the incidence of hypertension following short duration of toxemia be increased. The author's table shows that this is not the case. The relation between the duration of toxemia and the incidence of residual hypertension remains the same in both groups of patients. This is strong evidence against the second interpretation, and leaves us with the conclusion that longer duration of toxemia causes a rising incidence of consequent hypertension. The fact that this relationship may be graphed to yield a fairly regular rising line is hard to interpret on any other basis than that prolonged toxemia probably does cause hypertension.

(As noted in this abstract, it is the opinion of Dieckmann that a post-toxemic patient who still shows hypertension, proteinuria or impaired renal function 6 months or more after delivery, represents, and did represent in her hypertensive pregnancy, a state of chronic hypertensive vascular disease or vascular-renal disease. He believes that such a patient either had hypertensive disease before pregnancy or a predisposition to it by inheritance or by physical or mental instability (nervous and highstrung) and that the pregnancy was the exciting factor. The other point of view on this question which is shared by Chesley, myself and others, is that preeclampsia and eclampsia represent an acute vascular process in the form of vasospasm which, if allowed to continue for several weeks or so, results in a permanent structural injury to the vessel wall through anoxia,—an injury which makes itself manifest by arteriolar fibrosis and consequent hypertension. Although this might seem a simple matter to settle, cogent arguments may be advanced on both sides of the question and in the present state of our knowledge it seems difficult to prove or disprove either contention. Chesley's careful analysis of his 2 groups of post-toxemic patients would seem to be a logical approach to the problem and adds great weight to the school of thought which he represents. However, whether or not the acute toxemias actually cause subsequent chronic hypertension, there is general agreement from a clinical standpoint that the outlook both for mother and infant is improved if the acute toxemic process can be abbreviated.—Ed.)

DIURETIC EFFECTS OF ESTROGENS IN THE LAST FOUR MONTHS OF PREGNANCY

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Canad. M. A. J., 59: 431-434 (Nov.) 1948

The problem of excessive weight gain during pregnancy concerns both the doctor and the patient; to the former it suggests an impending toxemia, and to the latter it means wardrobe troubles, ungainliness, and strained arches causing painful feet. Because it is known that excessive weight gain is largely due to retention of fluids within the tissues, although true edema may not be demonstrable, the usual therapeutic measure which is taken to produce an outpouring of fluid is the administration of magnesium sulfate to cause watery stools and a concomi-

tant weight reduction. It is felt by the writer that the diuresis in the pregnant woman should be brought about by less drastic and more physiologic means. Despite the generally accepted theory that estrogens cause fluid retention, it was found that the administration of small doses of this substance is accompanied by control of the pregnant patient's weight.

In the matter of weight gain, pregnant women were divided into 3 classes: (1) those patients having the normal amount of weight gain for pregnancy; (2) those with rapid gain over a shorter period with overt edema and later toxemia; and (3) those who gain excessively despite restrictions in diet, salt and fluid intake, yet show no signs of toxemia. It is the third group which was under study in this paper. The majority of patients received 2 mg. of benzzestrol by mouth and 3 cases were given estrone sulfate (1.25 mg.) and 3 received ethinyl estradiol (0.05 mg.). Results were based on a study of weight charts and urinary output records.

Forty-three cases were given estrogenic substances but 3 cases were discarded as labor began before the patients were seen again. It was not felt that the estrogens influenced the initiation of labor. Two of 3 patients who later developed mild toxemia showed limitation of weight gain but the treatment was not continued. Only 2 patients in this series showed an added weight increment while on estrogens, and 5 other patients responded poorly to therapy. The remaining 29 patients showed adequate limitation of weight within 14 days after treatment was begun, and diuresis was evident in these patients. No deleterious effects were noted from the administration of estrogens and no effect on labor was apparent.

The author points out the numerous variable factors in a study such as this, and draws attention to the difficulties in running any type of a control series. Variations of weight which are within normal limits occur frequently and often unexplainedly in all trimesters of pregnancy. However, in view of this study, it is believed that further investigations of the estrogenic substances as related to fluid retention are warranted. 8 figures.

(As the author avows, her concept that the administration of estrogens may release edema fluid in pregnancy, contradicts all previous experience. Thus, Taylor and his associates, on the basis of extensive studies, believe that the steroidal sex hormones, especially the estrogens, are the main cause of sodium and water retention in pregnancy (*Am. J. Obst. & Gynec.* 38: 748, 1939; *idem* 45: 547, 1943). The evidence that these hormones do cause sodium and water retention is considerable. Thus, Thorne and Engle have injected estrone and estrial into dogs and have observed a decreased excretion of sodium (*J. Exper. Med.* 68: 299, 1938). Likewise, Friedlander and his associates have found that estrogen administration was followed by sharp rises in the blood volume in both human subjects and in cats (*Endocrinology* 20: 329, 1936). The sodium retaining effect of the estrogens and progesterone has already been given a clinical application in an explanation of the so-called menstrual edema by Thorne, Nelson and Thorne (*Endocrinology* 22: 155, 1938).

But all this evidence in opposition to Dr. Black's viewpoint does not necessarily mean that she is wrong,—no, not in this muddled field of the endocrinology of pregnancy where right-about-faces seem to be the order of the day. In the December issue of the Survey (p. 782) we were told that progesterone, long regarded as a uterine sedative, is actually an oxytocic; and in an abstract in the present issue (p. 190) we are informed by Dr. Olive Smith

that diethylstilbestrol, long considered of oxytocic potentialities, is the best therapeutic agent in habitual abortion. These 2 statements about progesterone and diethylstilbestrol, respectively, are in direct contradiction of opinions which were staunchly held just a few years ago. Now if Dr. Black's observations can be substantiated, still another reversal of judgment will confront us. All of which makes me wonder whether any of us really knows very much about the complex interaction of the endocrines in pregnancy.—Ed.)

EFFECT OF SEDATIVES ON URINARY VOLUME OF PREGNANT WOMEN

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J. Lab. & Clin. Med., 33: 1465, (Nov.) 1948

Edema is one of the cardinal findings in toxemia of pregnancy. In a previous paper, the authors reported the effectiveness of various diuretic agents in the mobilization and excretion of sodium and water. The present report concerns their observations on the antidiuretic effect of morphine and other sedative drugs in pregnant women.

A series of patients was given a constant intravenous infusion for 5 hours and hourly urine specimens were obtained for 8 hours. On test days these patients were given injections of a sedative, and the effect on urinary output and chloride excretion was measured. Morphine reduced the urinary output by 50 per cent without any significant alteration in total urinary chlorides. Fluid retention was further manifested by a transitory increase in body weight.

Another series of patients was given oral fluids as a liquid breakfast of 1,000 cc. between 7:00 and 8:00 A.M. Urine volumes were then measured at hourly intervals for 4 hours. On test days the sedative was administered one hour after the liquid breakfast. Morphine, Demerol, codeine and Amytal caused similar depression in urinary volume. Paraldehyde and Avertin were not found to have an antidiuretic effect.

It has been reported that morphine caused a release of the antidiuretic hormone from the pituitary in dogs. Studies were undertaken to determine the mechanism of this antidiuresis in women. The similarity of response by normal subjects and patients with diabetes insipidus to morphine suggests that this antidiuretic effect is not mediated through the posterior pituitary. Since hypnotic sleep did not induce this response, it is apparent that the antidiuresis was effected by some mechanism other than sleep itself.

These observations suggest that morphine and similar drugs should be used with caution in edematous states.

(Back in the late teens of the century when the old New York Lying-in Hospital was flourishing, eclamptic patients in that institution received the following medication: $\frac{1}{2}$ gr. of morphine sulfate on admission followed by $\frac{1}{4}$ gr. every hour until the respirations fell to

8 per minute (Ross McPherson, *Am. J. Obst. & Gynec.* 4: 50, 1922). During about the same time Beck was employing an identical regime and states that 1 of his patients received $\frac{1}{4}$ gr. of morphine within 16 hours without any harmful effects on mother or child (*Am. J. Obst. & Gynec.* 7: 677, 1924). Morphine in substantial dosage constitutes also of course an important part in the Stroganoff regime. And figures can be adduced to show that over the era when eclamptic patients were treated largely with morphine, the results were very good for that period, namely, a maternal death rate between 10 and 15 per cent.

The record of morphine in eclampsia is hence an old and satisfactory one and in view of this record it is difficult to believe that the drug can be so very harmful to eclamptic patients if administered with reasonable restraint. The authors of the above article are therefore wise in not condemning its use altogether and they recommend merely that it be used with caution. Because of its sedative effects, quick action and ready availability, morphine offers obvious advantages as an initial therapeutic agent in eclampsia. It is the drug most often given at the patient's home to allay convulsions during transport to the hospital, or in the admitting room of the hospital pending the institution of other types of medication. Morphine may be given also in the subsequent course of the therapy, but as the above authors point out, it is advisable to rely largely on other drugs for the main sedative program since, when administered repeatedly in large amounts, morphine not only reduces urinary output but also increases intracranial pressure and tends to cause acidosis because of decreased elimination of carbon dioxide from the lungs.—Ed.)

THE PHYSIOPATHOLOGY OF ECLAMPSIA

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Am. J. Obst. & Gynec. 57: 97-105, January, 1949

Five toxemic women died on the service of the authors during a 9 months period as a result of, or in association with, pulmonary edema. This motivated a change in treatment schedules and a simple policy of fluid maintenance was adopted. The daily fluid intake, therefore, is now limited to 2500 cc. No other treatment feature was changed and the basic philosophy of ultraconservatism was continued. Since then, no toxemic patient has died and none has developed recognizable pulmonary edema. Twenty-four consecutive pregnant women with convulsive toxemia have recovered and there is a 78 per cent fetal survival rate.

The current treatment for convulsive toxemia employed by the authors is summarized herewith. Upon admission, or after the initial convulsion, $\frac{1}{4}$ gr. of morphine sulfate is injected intravenously and $\frac{1}{4}$ gr. subcutaneously. Additional drug is administered (with 30 minutes between treatments for time to observe effect) in order to reduce the respiratory rate below 14, but not below 10 per minute. Occasionally, an enema of 200 cc. of tap water containing 20 or 30 gr. of chloral hydrate is substituted to avoid morphinization. External stimulus such as bright light, noise, needle pricks and catheterization, is avoided. A medical student remains in constant attendance. *Fluid intake is limited to replacement of*

the daily insensible loss (assessed at 1500 cc.) plus an amount equivalent to the urinary excretion of the previous 24 hours. This is not dehydration treatment; rather it is a policy of maintenance of fluid balance. Five per cent dextrose in distilled water is the standard infusion medium, and no hypertonic solution or plasma is employed. The obstetric status is ignored during the convulsive phase and treatment conducted without regard for the pregnancy. After convulsions are controlled and the patient becomes conscious, sedation is achieved with phenobarbital. The patient remains absolutely in bed, and generally accepted dietary principles, including high protein and low salt content, are followed. Labor is induced by rupture of the bag of waters 2 or preferably 3 days after the last convulsion. No ancillary treatment is employed, and operative delivery is performed only upon obstetric indication.

It seems that avoidance of excess injection of fluid has improved the recovery rate of the authors. If this be true, and not the result of chance, why are toxemic patients sensitive to fluid overload? Arteriolar spasm provides a satisfying answer to the question. There is irritability, but no resiliency of the muscular walls of the arterioles, with marked decrease of ability to accommodate fluid injected into the vascular tree. Moreover, the rate of water excretion by the kidney is seriously curtailed as a result of glomerular ischemia. These combine to make the toxemic woman resistant to sudden increase of blood volume. Right heart failure with pulmonary edema can, therefore, follow injection of a much smaller volume of fluid than is the case with a normal individual.

(I remember seeing an eclamptic patient many years ago who was recovering very nicely 2 days postpartum when she was given 4500 cc. of 10 per cent glucose intravenously over an 18 hour period. Forthwith edema of the lungs developed and she died. The warning which Mengert and his associates sound was apparently prompted by similar experiences and is fully justified in my opinion. It should also be remembered that the everlasting bedeviling of eclamptic patients with needles may do more harm than good.—Ed.)

THE MINIMAL SODIUM DIET. A CONTROLLED STUDY OF ITS EFFECT UPON THE BLOOD PRESSURE OF AMBULATORY HYPERTENSIVE SUBJECTS

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J. Lab. & Clin. Med., 33: 1482, (Nov.) 1948

A diet rigidly restricted in sodium is difficult to administer successfully to ambulatory hypertensive patients and a controlled evaluation of the factors attendant upon the use of this diet is necessary. Twenty-one hypertensive subjects were placed on a calorically adequate diet estimated to contain less than 300 mg. of sodium per day and were followed for about 18 weeks. Blood pres-

tures were obtained by a constant technique and 24-hour urine collections were made once weekly. All subjects received medication, consisting either of 4 Gm. of NaCl a day or of identical appearing placebos. After each 6-week period the medication was changed or continued according to prearranged schedules selected for each patient by the pharmacist.

The experiment thus consisted of 3 periods: during one or 2 periods supplemental sodium chloride was administered, while in 2 or one period the sodium intake remained at a bare minimum. During the study, neither the patients nor the investigators knew which medication was being taken.

Data from which evaluation of the effect of rigid sodium restriction upon blood pressure could be based were available from 8 subjects. The criteria for their selection required that the 24-hour urinary sodium average below 500 mg. for at least one period and over 1,000 mg. for at least one period. The average blood pressure taken during the rigid sodium restriction was lower than the average during the periods of added sodium, by 4.72 mm. Hg. diastolic and 4.96 mm. Hg. systolic. These differences are statistically significant.

DIETHYLSTILBESTROL IN THE PREVENTION AND TREATMENT OF COMPLICATIONS OF PREGNANCY

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Am. J. Obst. & Gynec. 56: 821-834, November, 1948

The basis for the use of stilbestrol in pregnancy is briefly reviewed, together with the indications and the dosage schedule recommended. Complete case reports on 632 pregnant women, to whom diethylstilbestrol was given largely for the indications and in the amounts recommended in the author's clinic, have been analyzed. They have been divided according to the indications for therapy, i.e., threatened abortion (219 cases), abortion prophylaxis (272 cases) and prophylaxis against late pregnancy toxemia, intrauterine death, and premature delivery (98 cases). Although the author has not recommended stilbestrol as a definitive measure in later pregnancy, 24 patients were so treated and are considered separately. Nineteen cases that fell into none of these categories are omitted.

Seventy-eight per cent of the patients who were treated for bleeding between the 6th and 21st weeks carried to 28 weeks, and 72 per cent had living and well babies. The highest spontaneous cure rate reported in the literature is 50 per cent. Eighty-three per cent of the patients who were given stilbestrol prophylactically against abortion carried to 28 weeks, and 78 per cent had living and well babies. In the 127 cases who had had 2 to 5 consecutive abortions prior to the one in which stilbestrol was given, the fetal salvage averaged 77 per cent.

In each group it was very significantly higher than the spontaneous cure rate as established by Malpas and Eastman. In the total 491 cases treated for abortion the incidence of abortion and of later pregnancy complications was higher when the dosage schedule was not followed than it was in the group as a whole.

In many of the patients treated prophylactically for late pregnancy complications it was impossible to evaluate the effect of stilbestrol therapy, and this part of our report must be considered preliminary. Twenty-two of them, however, had had 3 or more previous obstetric abnormalities, 27 had had 2 or more premature deliveries, 17 had known essential hypertension with bad obstetric histories, and 9 had diabetes, 6 of these with bad obstetric histories. Considering the past obstetric histories of these patients, the course and outcome on stilbestrol gave good indication that the administration of this drug as a preventive measure may be expected to reduce the incidence of those complications of later pregnancy associated with a premature deficiency of the placental steroid hormones, estrogen and progesterone. There was even stronger evidence that the onset of these complications would be postponed and the fetal mortality reduced. The results of the use of stilbestrol as a definitive measure in later pregnancy were not promising.

(The statistics on threatened and habitual abortion reported in this paper are the best that have come to my attention, being much better, as the author points out, than one could possibly expect on the basis of spontaneous cure rates. For instance, of 38 patients who had had 3 previous consecutive abortions, 87 per cent obtained living and well babies in their fourth pregnancies on the stilbestrol therapy with no supplementary treatment of any kind. Now it will be recalled that the accepted incidence of spontaneous abortion in general is 10 per cent of all pregnancies and that the lowest stillbirth and neonatal loss which most of us can achieve is around 2 or 3 per cent of all deliveries. Adding together these 2 sources of fetal wastage it will be seen that in any large number of presumably normal pregnant women, about 12 or 13 pregnancies will not come successfully to fruition. This is the exact figure which Dr. Smith reports for her women who had had 3 consecutive abortions previously; in other words, under stilbestrol treatment the habitual aborter enjoys the same outlook for a living baby as does the average gravida. This is what I mean by saying that these statistics are the best that have been reported. In fact, they couldn't possibly be any better.

No mention is made in this paper of thyroid therapy and in the chronic aborter group it is expressly stated that no supplementary therapy was given,—merely stilbestrol. Yet in these 127 patients who had had 2 to 5 consecutive abortions, one would surely expect to find a substantial proportion with thyroid deficiency. It has been found in our Clinic that thyroid deficiency is encountered more frequently as the degree of habitual abortion augments, being 37 per cent in cases with less than 3 abortions and 70 per cent in true habitual aborters with 3 or more consecutive abortions (Eleanor Delfs, *Obst. & Gynec. Surv.* 3: 680, 1948). The fact that none of Dr. Smith's large series of habitual aborters appeared to need the thyroid is perplexing. Is it possible that a tie-up exists between stilbestrol and thyroid so that the former can substitute for the latter in so far as reproductive deficiency is concerned?

For the sake of brevity the above abstract does not include mention of the way in which the statistics were collected. The data were received from 117 obstetricians who not only followed the author's recommendations but were willing to pool their results and send her a complete record of each treated case. In order to be certain of procuring a record on every treated patient, each doctor, upon receiving an allotment of stilbestrol, was required to send in a card for each patient to be treated, stating the name of the patient, the last

menstrual period, and the indication for therapy. These cards were filed under the doctor's name according to the expected date of confinement. Final record sheets were also supplied and, if not returned soon after a patient was due to deliver, follow-up letters were sent to the obstetrician. In this way the author hoped to be sure of receiving records on all treated patients and to overcome the tendency of any busy practitioner to forget short periods of therapy that terminated in failure. She believes that she has been fairly successful in this, since her only incomplete records to date are on patients who moved away in the middle of a pregnancy and could not be traced by their obstetricians. She points out, however, that there is a possibility that cards were not sent in on all cases. In tabulating the data, however, she has analyzed all past pregnancies of these patients and used this means of evaluating results. I can see offhand no great source of error in this method of collecting data, but there may be.

The dosage scheduled was 5 mg. of diethylstilbestrol daily by mouth started during the 6th or 7th week counting from the start of the last menstrual period. The daily dosage was increased by 5 mg. at 2 week intervals to the 15th week when 25 mg. daily were being taken. Thereafter, the daily dosage was increased by 5 mg. at weekly intervals. Administration is discontinued at the end of the 35th week since a drop in estrogen and progesterone normally precedes the onset of labor. The dosages prescribed are not large enough per se, in the author's opinion, to raise the estrogen level above the physiologic norm of pregnancy and it is emphasized that stilbestrol is given not because it is estrogenic but because it stimulates the secretion of estrogen and progesterone.—Ed.)

HYDATIDIFORM MOLE AND CHORIONEPITHELIOMA

E. NOVAK

Am. J. Surg., 76: 352-353, (Oct.) 1948

Hydatidiform mole is a relatively rare condition, its incidence being about one in 2,000 pregnancies. Chorionepithelioma, however, is exceedingly rare, and if one looks over the reported cases in the literature, it is evident that in many of these there have been errors of interpretation, and that a not inconsiderable portion of them were instances of benign although perhaps proliferative types of hydatidiform mole.

There is no field of pathology in which diagnostic mistakes are more common than in this, and such errors have all too often led to unnecessarily radical plans of treatment. Further elements of confusion have recently been added through overemphasis on the diagnostic and prognostic significance of the biologic tests which, valuable though they are, should be looked upon as adjuvants in clinical evaluation.

While the frankly benign and frankly malignant cases offer no difficulty in microscopic differentiation, there is a borderline group in which there will be uncertainty in the minds of even highly trained pathologists. To this intermediate group have been applied such designations as malignant mole or chorioadenoma destruens. Efforts at correlating the histologic and clinical characteristics of such moles, chiefly on the degree of trophoblastic proliferation or on the degree of anaplastic activity, have thus far not been satisfactory.

The difficulty lies in the fact that even a normal trophoblast exhibits many of the characteristics commonly associated with malignancy. It destroys and invades the maternal tissues, penetrates the blood vessels and even undergoes a species of normal or physiologic metastasis as can be seen in the process of deportation of trophoblastic villi to the lungs; this probably occurs in all normal pregnancies.

However, the maternal tissues, presumably through the agency of the decidual cells, exhibit a defensive mechanism which holds the trophoblastic encroachment within normal limits. A deficiency in this defensive mechanism may be more important than abnormal trophoblastic activity in the explanation of the abnormal vascular penetration which characterizes the so-called malignant mole. On the other hand, it is quite likely that this defense mechanism explains the spontaneous local regression and even complete cures which have been reported in occasional cases of genuine chorionepithelioma.

There is now general appreciation of the fact that a high quantitative gonadotrophic titer is not by any means decisively important in diagnosis, chiefly because this diagnostic problem usually arises at that phase of pregnancy in which there is normally a high peak of gonadotrophin production. Much more important is the biologic follow-up after evacuation of the mole although this too offers possible pitfalls.

If a high titer persists, it is always better to do a repeat curettage, especially as this generally can be carried out more safely and thoroughly now that the uterus is smaller and firmer. Often the curettage will reveal further molar tissue, but sometimes not. In either case if a high or increasing titer persists beyond this, one is fully justified in performing a hysterectomy.

This may reveal a definite chorionepithelioma but in most cases it will not. Microscopic examination of the uterus reveals more often trophoblastic tissue, often with large molar villi, deep in the uterine wall and sinuses. However, the hazard in such cases is so great that the radical procedure is fully justified.

The writer has set forth these comments to call attention to the many problems still surrounding this general subject along pathologic, diagnostic and therapeutic lines. For this reason, the American Association of Obstetricians, Gynecologists and Abdominal Surgeons recently created the Albert Mathieu Chorionepithelioma Registry. The accumulation, study and follow-up of the cases submitted to this Registry should in time yield worthwhile results in the elucidation of some of the problems indicated in this paper. It is sincerely hoped also that gynecologists and obstetricians throughout the country will join in this cooperative undertaking by sending to the Registry material and clinical data from cases of hydatidiform mole and chorionepithelioma from their own practices and clinics.

CHORIONEPITHELIOMA TREATED WITH STILBESTROL

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Lancet, 254: 944-945, (June 19) 1948

The case reported is that of a 20-year-old white woman, gravida 2, who in December of 1944 spontaneously expelled a hydatid mole. Following this, she had irregular metrorrhagia and curettage was performed in November, 1945, and in January, May and June, 1946. Early curettage revealed endometritis and decidual remains but in June chorionepithelioma was found.

On examination the uterus was found to be enlarged and of a soft consistency. Radiography of the lungs showed very small metastases. The pregnancy test was positive and the gonadotrophic hormone level in the urine was 333 to 4200 mouse units per liter.

An abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. Two chorionepitheliomas, measuring about $1\frac{1}{2}$ inches in diameter, were found in the fundus. Deep radiotherapy was given postoperatively but was discontinued since the patient apparently was going downhill. She complained of chest pain and cough. She was started on stilbestrol, at first 3 mgm. per day, and this dose was gradually increased to as high as 1000 mgm. per day. This therapy caused a reduction of the gonadotrophic hormone level and marked improvement in the respiratory symptoms. Chest x-ray showed some regression of the lung lesion when she was placed on large doses. The patient developed a severe vaginal infection at the site of a metastasis which produced hemorrhage, anemia and death 6 months after stilbestrol therapy was begun.

At autopsy the outstanding findings were the evidence of widespread metastases and changes in the hypophysis. Many of the basophilic and eosinophilic cells were small and shrunken with pyknotic nuclei and degeneration. There was no evidence of hepatic necrosis. There were no histological changes in the tumor cells.

The writer feels that this form of treatment might prove of value if the stilbestrol were given in large enough doses and early enough. It seemed to be of special value in relieving the symptoms of the metastatic lesions.

ANGINA OF EFFORT IN PREGNANCY. (REPORT OF A CASE)

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J. Obst. & Gynaec. Brit. Emp., 55: 428-431, (Aug.) 1948

The case is presented of a 37-year-old woman, 3 months pregnant, who was seen because of precordial pain. The patient had always been highly strung and was prone to palpitations. The attacks of pain were brought on by excessive lifting or walking or by getting into a cold bed. The pain would last only a few seconds and disappeared on rest.

At the time of examination the woman appeared excitable and sighed frequently. Apart from a short systolic murmur over the apex and base and a slight accentuation of the second pulmonary sound, no abnormalities were found on physical examination. The blood pressure was 145/85. Chest x-rays showed no marked changes. A resting electrocardiogram showed a sinus rhythm, rate 81, left axis deviation and lengthening of the A-V and interventricular conduction time (P-R: 0.22, QRS: 0.1-0.11 sec.). An exercise test showed diminution of exercise tolerance with early dyspnea and chest pain. Subsequent electrocardiograms taken 1 to 7 minutes after the test showed evidence of myocardial anoxia.

The patient was carried to term on supportive therapy and she was able to carry on with household duties without undue discomfort. She was delivered by cesarean section for obstetrical reasons. One year following delivery the patient was in good health with only occasional attacks of pain after excessive exercise. The electrocardiographic changes seen earlier continued both at rest and after exercise.

As the writer was unable to find previous reports concerning the electrocardiographic changes in pregnant women after the exercise test, 7 other pregnant women who had no cardiac disease were tested in a like manner. None of these patients showed any evidence of myocardial anoxia.

Angina in pregnancy is a rare combination, primarily because angina in any woman under 40 years of age is exceedingly uncommon. It has been described in pregnancy when associated with organic heart disease which caused aortic regurgitation. Coronary occlusion has also been described as occurring during pregnancy, but this too is a very unusual finding.

PLACENTA PRAEVIA ACCRETA

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J. Obst. & Gynaec. Brit. Emp., 55: 470-472, (Aug.) 1948

The case is reported of a 35-year-old woman who was admitted to the hospital at, or somewhat beyond term with vaginal bleeding. She had one child, aged 5 years. Past history revealed that she had had repeated attacks of menorrhagia since delivery of her first child. A curettage had been performed because of this menorrhagia. The present bleeding occurred shortly after a vaginal examination by her local physician who then immediately hospitalized the patient. On admission, her general condition was good. The uterus was enlarged to the size of a 34-week pregnancy and fetal heart sounds were heard. Vaginal examination was repeated at the hospital and a diagnosis of central placenta previa was made. A lower uterine cesarean section was performed and a living male child was delivered. Search for a line of cleavage between the placenta and the uterus proved unavailing, and free and alarming bleeding was then encountered. As much of the placenta as possible was removed piecemeal and the operation was completed without further difficulty, although at the time it was not felt that all of the placenta had been removed. The infant died 8 days postpartum of congenital heart anomalies and gangrene of the ileum.

On the sixteenth and seventeenth postpartum days there was slight loss of blood. On vaginal examination the cervix was found to be still open. Several small pieces of placenta were removed but such free bleeding was encountered that the examination was stopped and a firm cervical pack was inserted. Two days later, on removing the pack, an alarming hemorrhage occurred and a total hysterectomy was immediately performed. The patient did well postoperatively and was discharged on the fifty-sixth day.

Pathological examination showed several cotyledons of the placenta infiltrating deeply into the wall of the lower segment and their removal was impossible. Microscopically, there was complete absence of the decidua basalis. Nitabuck's layer was ill-defined and the villi lay mostly on an edematous muscle layer. Many of the villi were degenerated and there were thromboses in the maternal sinuses and fetal villi.

The author has reviewed the etiologic factors in placenta accreta and suggests that the previous curettage may have been a factor in this case. He also points out that the so-called adherent placenta tends to recur, and this condition may represent a mild degree of placenta accreta. It is uncommon for placenta accreta to occur previa, and in the review of Irving and Hertig placenta previa occurred in 13 instances in 86 cases of placenta accreta. When previa does occur it carries a higher mortality rate. Treatment of these cases is a difficult problem, for often partial separation has occurred. The only safe treatment is hysterectomy as soon as the patient's general condition justifies it. In view of the

fetal abnormalities the author wonders how much the fetal circulation is impeded in placenta accreta, and what would be the possible secondary effects on the fetal cardiovascular circulation.

ACUTE HYDRAMNIOS

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Am. J. Obst. & Gynec. 56: 1069-1076, December, 1948

Acute hydramnios is apparently very rare. Bequain (Quoted by Goldschmidt. *Ztschr. f. Geburtsh. u. Gynäk.* 87: 551, 1924) determined that it occurs once in 12,000 deliveries. O'Driscoll (*J. Obst. & Gynaec. Brit. Emp.* 52: 496, 1945) reviewed the reported cases in the literature and found only 90 which could be classified as acute. Chronic hydramnios, on the other hand, is much more common. Tweedy (*J. Obst. & Gynaec. Brit. Emp.* 10: 101, 1906) has reported an incidence of one in 262 deliveries, and Ryder (*Am. J. Obst. & Gynec.* 24: 784, 1932) one in 177 deliveries. In the present study there were 4 cases of acute hydramnios in 49,793 deliveries at the New York Hospital, an incidence of 1 in 12,448, a figure closely approximating that of Bequain.

The material for this study was gathered from a review of charts of 115 cases in which a tentative diagnosis of hydramnios was made by any one observer in the antepartum clinic or in the hospital. If subsequent examination of any individual patient in the clinic or hospital did not again suggest hydramnios, the case was discarded from this series. On that basis 49 cases were excluded from the present presentation. Of the remaining 66 cases, it was felt that 4 corresponded to the type referred to in the literature as acute hydramnios.

There is another larger group of cases in which the accumulation of an excessive amount of amniotic fluid is more gradual. The patient is able to compensate for the reduced thoracic capacity, and does not necessarily suffer acute respiratory distress. The pregnancy usually continues to term, and the fetal mortality is much lower. This type has been called moderate or chronic hydramnios. There were 62 cases in the present series which corresponded to this type, an incidence of 1 in 794. Three of these occurred in twin pregnancies. There were 14 cases, or 23 per cent, in nulliparous patients, and 48, or 77 per cent, in multiparous patients.

The prognosis for the infant in hydramnios has always been recognized as being very poor. Krahula (*Monatschr. f. Geburtsh. u. Gynäk.* 55: 199, 1921) reported a series of 207 cases of hydramnios from the Bonn Clinic and stated that a total of 28 children left the hospital alive and healthy. Floris, (*Monatschr. f. Geburtsh. u. Gynäk.* 62: 55, 1923) in a study at the Kermauner Clinic in Vienna,

reported 236 cases from which 183 infants were born viable and were discharged from the hospital in good condition. Ryder (Am. J. Obst. & Gynec. 24: 784, 1932) reported that of the 141 infants delivered in his 113 cases, there were 76 survivals.

Of the 65 infants (3 cases of twins) in the present review of chronic hydramnios, 31, or 48 per cent, were born alive and left the hospital in good condition. Of the 34 infants which did not survive there were 17 deadborn, 10 stillborn, and 7 neonatal deaths. In Table III the causes of the fetal deaths are given.

The fetal mortality was 100 per cent in the 4 cases of acute hydramnios. The uncorrected fetal mortality in the chronic cases was 52 per cent. Of the 34 infants which did not survive, 19 had congenital abnormalities, 7 had erythroblastosis and 8 were otherwise normal.

The conservative approach to the treatment of hydramnios has always been more acceptable, such treatment consisting of rest in bed, limitation of fluids

TABLE III
Fetal Deaths

CAUSES	NO. OF CASES	INCIDENCE
Congenital anomalies.....	19	29.0
Anencephaly.....	12	
Achondroplasia.....	2	
Spina bifida and teratoma of the buttocks.....	1	
Hydrocephaly.....	3	
Congenital heart defect.....	1	
Erythroblastosis.....	7	11.0
Other causes.....	8	12.0
Total.....	34	52.0

and salt, and either medical induction of labor or rupture of the membranes from below if the maternal distress becomes too great. Since 1919, however, other forms of therapy have been reported in the literature. Chief among these is the aspiration of the amniotic fluid through the abdominal wall. The advocates of the abdominal aspiration method of treatment maintain it to be superior to the vaginal approach inasmuch as the danger of infection is thereby reduced. Furthermore, the release of the amniotic fluid abdominally can be so well controlled that labor does not ensue. They admit that there are many theoretical dangers, but contend that there has never been a serious accident.

Of the 39 reported cases there were 12 twin deliveries, making the total number of infants 51. Results with respect to the infant were not given for 16 of the 51 infants. Of the 35 infants in which the result was given there were 18 infants which did not survive. This gives an infantile mortality rate of 51 per cent.

X-ray diagnosis of anencephaly was made in 9 cases prior to delivery. Since it has been shown in this study and in the literature that there is a correlation between congenital anomalies and hydramnios, it is felt that x-ray examination

of the abdomen should be performed in all cases in which hydramnios is diagnosed. Abdominal aspiration of the amniotic sac was not performed in any of the cases. Abdominal aspiration of the amniotic fluid perhaps should be reserved for those cases of acute hydramnios in which maternal distress is so great that intervention before viability of the fetus is indicated. In the author's reported series this condition arose once in 12,448 deliveries. He believes that abdominal aspiration should never be performed in cases of chronic hydramnios.

(In regard to the abdominal aspiration of amniotic fluid in cases of extreme hydramnios, see editorial note in December, 1948 issue of the Survey, page 786.—Ed.)

TORSION OF HYDROSALPINX IN PREGNANCY

J. HADLEY

Lincoln, England

J. Obst. & Gynaec. Brit. Emp., 55: 335-336, (June) 1948

The case is presented of a 23-year-old female, 4 months' pregnant, who was admitted to the Lincoln County Hospital with the complaints of generalized abdominal pain and nausea and some vomiting which had been present for 4 days. Shortly after admission, the pain became localized to the left iliac fossa. On examination, the only positive findings were slight abdominal distension and uterine enlargement corresponding to a 4 months' pregnancy. The leukocyte count was 15,000; the sedimentation rate was 15 mm. per hour; the urine contained a moderate amount of pus cells but was sterile on culture. X-ray of the chest showed a shadow at the base of the right lung which raised the possibility of tuberculosis. After about 6 days in the hospital, it was possible to feel a fluctuant tumor in the left iliac fossa and the uterus was displaced to the right. At operation a black "cyst-like" mass was found in the left iliac fossa adherent to the pelvic wall and to the colon and arising in association with the Fallopian tube. The tube had undergone $1\frac{1}{2}$ to 2 twists. A salpingectomy was done. The remaining adnexa were normal. The specimen was a cyst-like mass, 4 inches in length, and was found to consist of a grossly dilated tube, thin-walled and full of blood-stained fluid and a little clot. The patient made an uneventful recovery and delivered normally at term.

A review of the literature suggests that this condition is rare and is more commonly unassociated with pregnancy. The most recent comprehensive review was made in 1927 by Eastman, 91 cases being reported at that time. Torsion of a normal Fallopian tube has been described in adolescent girls in whom existing hydrosalpinx would seem unlikely. Others have maintained that the tube is the seat of a hydrosalpinx which is converted into a hematosalpinx after torsion. It may occur in virgins, in the absence of a history of infection, as a sequela of vulvovaginitis in childhood which remains latent until puberty, as a late result

of an unrecognized salpingitis or as a result of an attenuated tuberculous infection. It is necessary to differentiate this condition from obstruction of the bowel, torsion of an ovarian cyst, ectopic pregnancy, appendicitis, renal conditions and a cold abscess.

PREGNANCY ASSOCIATED WITH A SEPTATE UTERUS, DOUBLE VAGINA AND OTHER CONGENITAL ABNORMALITIES

JEAN R. C. BURTON-BROWN

University of Oxford

J. Obst. & Gynaec. Brit. Emp., 55: 418-422, (Aug.) 1948

The various types of congenital abnormalities which may occur in the female genital tract are described and the author draws special attention to the fact that when one abnormality exists, it is highly probable that others will be found, not only in the urinary tract, which is closely associated with the genital tract in its development, but in other parts of the body. Wharton (1925) states that the study of a patient with malformation of either reproductive or urinary organs is fundamentally incomplete unless investigation includes the whole genito-urinary system.

Regarding the frequency of uterine anomalies, Smith (1931) recorded that whereas only 16 cases were described in general hospital records over a 26-year period (1 in 7,040), no less than 19 cases (1 in 1,458) were observed by himself in careful examinations over a period of 5½ years, showing that in all probability many cases passed unnoticed in the former group. Taylor (1943) found that complete or incomplete lack of fusion of the Müllerian ducts arises in about 1 in 1,500 cases from obstetrical wards and 1 in 2,000 from gynecologic wards.

Way records the following complications in 32 pregnancies with uterine anomalies: transverse lie, 12; abortion, 12; breech delivery, 4; premature labor, 3; placental retention, 3; prolapse of cord, 2; and placenta previa, 2. The incidence of postpartum hemorrhage has been reported as higher in cases of uterus arcuatus than in normal uteri. Uterine rupture is also a complication. Twin pregnancy is said to occur more commonly in cases of double uterus. In the case of an abnormal kidney, pregnancy may light up an incipient pyelonephritis or glomerulonephritis. It is possible that pre-eclampsia may also occur more frequently because of deficiency of renal function.

The author presents the case of a 31-year-old unmarried woman, 16 weeks pregnant, who was referred because of bilateral congenital dislocation of the hips; the problem was whether termination of pregnancy should be considered.

The menses were regular but there was extreme menorrhagia. Examination revealed albuminuria. The blood pressure was 120/80. A septum was visible

at the introitus, dividing the vagina into 2 lateral components. A softened cervix was felt in each vaginal vault. A cystic swelling arose from the right cervix and a smaller but firm, irregular swelling connected with the left cervix. A diagnosis of double uterus was made, with a pregnancy in the right uterus and several small fibroids in the left uterus. The anus was absent, the rectum opening into the posterior part of the vulva.

X-ray examinations showed a fetus of 4 months' maturity presenting by vertex, bilateral congenital dislocation of the hips, and congenital deformity of both kidneys amounting to a horse-shoe kidney, the ureter absent on the right side.

It was decided to terminate the pregnancy on the basis of albuminuria appearing at an early stage of pregnancy and the probable impairment of renal function. The patient did not desire marriage or children, and wished to have the uterus removed in order to be free of her distressing menorrhagia. A hysterotomy was performed in order to confirm the presence of a septum, followed by total hysterectomy. Small fibromyomata were dotted about the nonpregnant uterus and one or two were present in the other uterus. Both ovaries and tubes appeared normal and were conserved. The patient made an uninterrupted recovery. 4 figures.

HEART BLOCK AND PREGNANCY (A REVIEW)

R. MOWBRAY

University of Durham

J. Obst. & Gynaec. Brit. Emp., 55: 432-437, (Aug.) 1948

The author has reviewed 35 reported cases of heart block associated with pregnancy with a view to finding indications regarding diagnosis, prognosis and treatment. Twenty of the 35 cases were due to acquired heart block and 15 were congenital.

The causes of acquired heart block included acute infections (diphtheria, influenza, pneumonia, scarlet fever, typhoid and syphilis), rheumatism, trauma, and in a few cases no cause could be determined. In the 20 published cases, the ages ranged from 20 to 38 years, and the number of pregnancies from one to 8. The block was complete in 14 cases, partial in one, both partial and complete in 2, and not definitely known in 3. Over half of the cases were due to rheumatic infections. The immediate maternal mortality rate was 20 per cent, and it was impossible to state what effect pregnancy had on the course of the existing heart disease. It would appear that the presence of acquired heart block in a given case increases the danger of pregnancy, but it is the general cardiac state of the patient which is most important. Heart block alone in these cases does not seem to be an indication for termination of pregnancy.

Congenital heart block is probably not as rare as is supposed but it is over-

looked because of the relatively fast heart rate. Other cardiac abnormalities associated with block are interventricular septal defects, pulmonary stenosis, patent ductus arteriosus, dextracardia and atrial septal defects. However, the cases with other gross cardiac lesions do not often reach the childbearing age. The age range of the cases reviewed was 22 to 36 years and the number of pregnancies varied from 11 to 3. Heart block was complete in all but one case. Nine cases definitely or probably had interventricular septal defects and 5 cases had no other cardiac abnormality. Only 3 cases showed signs of heart failure and these were mild in nature. Stokes-Adams attacks were also mild and infrequent. Delivery presented no unusual problems and the postpartum progress was normal. There was no evidence to show whether pregnancy had any long term effect on the cardiac condition. The one patient who died developed toxemia and hypertension and then cardiac failure. It would seem that congenital complete heart block does not contraindicate pregnancy in the absence of cardiac failure.

The diagnosis of heart block depends upon a high index of suspicion in cases of bradycardia and other cardiac abnormalities plus the use of the electrocardiographic examination. The prognosis depends upon making an accurate etiological diagnosis, for the outlook is good in the congenital cases while acquired heart block carries a much higher maternal mortality rate.

(This is an important article on a rare but serious complication of pregnancy. In 1933, Jensen was able to collect only 14 cases from the literature and from this it is apparent that Mowbray's total of 35 cases represents a substantial number for this condition. As the author points out, the prognosis depends upon the general cardiac status, especially the frequency and severity of Stokes-Adams attacks. For further discussion of this complication, see editorial note in Survey, 2: 305, 1947.—Ed.)

THE PROGNOSIS OF THE CARDIAC PATIENT IN PREGNANCY

S. LESSE

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Am. J. Obst. & Gynec., 56: 477-483, (Sept.) 1948

This study was carried out on 203 pregnant women with some type of cardiac disease in order to determine the frequency of decompensation, the clinical value of the functional classification of heart disease, the relative importance of the age and parity factors in prognosis, and the relation of auscultatory findings to the frequency of myocardial failure.

In general it may be said that certain cardiac abnormalities contraindicate a contemplated pregnancy. The presence of marked cardiac decompensation during a previous pregnancy or evidence of moderate to marked cardiac failure during the nonpregnant period was the prime contraindication, and 71 per cent

of such patients developed heart failure again in pregnancy. In the total series of 203 cases 26.6 per cent decompensated at one time or another.

The functional classification, while it may be used to predict the increase in frequency of myocardial failure as one goes from Class I to Class IV, fails to explain the substantial number of patients in Class I and II that decompensate, though on the basis of this classification they were expected to have little or no difficulty during pregnancy. It would appear that a classification of heart disease having an anatomical as well as a functional basis would be more adequate. In this series, 12 per cent of the patients falling into the first two classes showed an unexpected decompensation during their pregnancies.

Age is an important factor in prognosis, for the frequency of myocardial failure in patients over the age of 30 years is more than twice as great as it is among patients of 30 years or younger. It also appears from the findings of this study that for women of the same age the factor of parity had little or no effect on the prognosis, unless there was a history of previous decompensation.

The mitral stenotic murmur is by far the commonest auscultatory abnormality affecting the prognosis of the pregnant cardiac patient. In this series, 55.9 per cent of the patients in Classes II, III and IV having mitral stenosis decompensated. Of the 54 cases in this series which decompensated, 47 occurred before labor, one during the course of labor and 6 in the puerperium. The 203 cardiac cases represent 3.2 per cent of 6285 consecutive pregnancies, with 3 cardiac deaths representing 15 per cent of the 22 patients that died of all causes during the period concerned.

(When a rheumatic heart disease patient in early gestation has a valid history of cardiac decompensation in the previous pregnancy, or if heart failure has occurred within the past year in the nonpregnant state, therapeutic abortion is indicated, in my opinion, if it ever is indicated. The author's statement that 71 per cent of such patients in his series developed heart failure again in pregnancy supports this viewpoint. It is instructive to note that 12 per cent of his Class I and II cases showed unexpected decompensation during their pregnancies. This serves to remind us that it is impossible to pigeon-hole patients in these classes and expect that they will stay there. As pregnancy advances, it now and then happens that a Class I case will show signs and symptoms which demand shifting her to the Class III bracket. This does not mean that the classification of the New York Heart Association is to be condemned or that the doctor who originally evaluated the cardiac status was necessarily at fault. After all, nothing in medicine is 100 per cent certain and if we are able on the basis of this classification to establish correct prognosis in 90 per cent of cases, this is something to be thankful for. The fact that a few of these patients may shift from one class to another as pregnancy progresses, however, calls to mind the necessity of vigilant observation of all gravidæ who are handicapped by valvular disease, even those who appear to belong in Class I.—Ed.)

DECIDUAL BLEEDING IN PREGNANCY

H. A. POWER

Pittsburg, Pa.

Am. J. Obst. & Gynec., 56: 743-750, 1948

Bleeding during the first five months of pregnancy can present a puzzling diagnostic problem. The elimination of threatened and incomplete abortions, tubal pregnancies, premature separation of placenta, placenta previa, and cervical pathology still leaves a group of patients with vaginal bleeding and normally progressive uterine enlargement. Gross evidence of an unhealthy decidua has been found in some of these patients. The pathology consists of degeneration with leucocytic infiltration of portions of the decidua vera, and often a plaque of such decidua is found adherent to the maternal surface of the membranes.

A study of 13 such cases in which bleeding was present in varying amounts was made. Brief abstracts of the 13 cases are presented. Seven patients were in the second, and 6 in the third decade of life. The menstrual history was abnormal in 7 and normal in 6 cases. The onset of symptoms began between 4 to 10 weeks in 11 patients and at 12 weeks in 2 patients. The bleeding occurred in varying amounts from slight to moderately profuse. Cramps and bleeding together seemed to offer a poor prognosis, as the duration of pregnancy after the onset of cramps was 4 weeks in 2 cases and 6 weeks in 2 others.

There were 3 stillbirths, one at 4½ months and 2 at 5 months. Ten babies, or 77%, survived. Viable survival was 100%. One baby was born at 7 months, 3 at 8 months, 3 at 8½ months and 3 at term.

There were 5 primigravidas and 8 multigravidas.

The initial diagnoses included: premature separation of placenta, 2; threatened abortion, fibroid uterus, 1; threatened abortion, 9; low implantation of placenta, 1.

One patient was fully ambulatory without any therapy, 5 were on bed rest alone and 7 were kept in bed and given estrogen and progesterone therapy. The final outcome of the pregnancies seem to depend on the extent of the decidual degeneration. There was no evidence of subplacental hematomas or gross placental pathology.

One of the patients presented an apparent cervical polyp, which was found to be degenerated decidua.

Normal progression of the pregnancy with gradual cessation of the bleeding, examination of any tissue passed, and inspection of the placenta and membranes following delivery will make the final diagnosis. The early elicitation of the fetal heart sounds is of diagnostic and prognostic value. Conservative management of these patients is indicated. The value of endocrine therapy seems questionable. 4 figures.

PREGNANCY COMPLICATED BY LARGE HYDRONEPHROSIS

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Preston, England

J. Obst. & Gynaec. Brit. Emp., 55: 499-500, (Aug.) 1948

The case is presented of a 36-year-old woman who had had one previous pregnancy which ended in abortion, and who was seen on this occasion at the 18th week of pregnancy. Her only complaint was swelling of the abdomen which she attributed to the pregnancy. On examination, she was found to have a large cystic swelling which filled the upper abdomen, lying above and to the left of the uterus. The urine was normal and the blood pressure was 110/70. A laparotomy was performed and the cyst was found to be extra-peritoneal, extending from the pelvic brim to the diaphragm on the left side. The colon was mobilized, the cyst was partially collapsed and shelled out with some difficulty. After removal of the cyst the left kidney could not be found and the right kidney was enlarged. The area was reperitonized, the abdomen closed and the patient made an uneventful recovery.

Pathologically, the wall of the cyst was lined in patches by cuboidal or flattened cells but definite kidney tissue was not found. On one side of the cyst was an almost obliterated tube which may have been a ureter. It was felt that the cyst was the end result of a hydronephrosis, even though the histology was not conclusive.

The pregnancy continued normally until the 37th week when the blood pressure rose to 140/90. The blood urea varied from 18 to 27 mgm. per cent. Labor was induced by rupture of the membranes at the 38th week and completed with a low forceps extraction. Postpartum the mother and baby did well. Prior to delivery there was a mild right hydronephrosis demonstrated by intravenous pyelogram. This disappeared after the baby was born.

AN INVESTIGATION ON PREGNANCY IN DIABETIC ANIMALS

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Acta path. et microbiol. Scandinav., 25: 131-140, 1948

The author has now assembled material consisting of about 20 cases of diabetic pregnancy in rats, and in this paper presents a preliminary report on his investigations.

In most instances, diabetes was produced in the animals by subtotal pancreatectomy and in a few cases by means of alloxan. The majority of animals

were operated on at varying times after the start of pregnancy. Blood and urine sugars were studied. Most of the animals were treated with insulin.

The clinical course of the diabetes in the mother rat varied widely in the different animals. In some animals the increase in the blood sugar was only slight, the values being around 0.15 g. per hundred cc. (normal value for this breed of rat is around 0.08 g.), whereas in others, figures around 0.4 g. were obtained. In a couple of the animals becoming pregnant after they had had diabetes for some time the blood sugar values rose during pregnancy, with a strong tendency toward fluctuation. A value as high as 1.45 g. per hundred cc. was obtained on one occasion from a pregnant alloxan rat. A strong decrease in the blood sugar generally occurs immediately before delivery. As a rule, there is an increase in the blood sugar during or after parturition. In these animal experiments there was no improvement in the diabetes of the mother rat during the later stages of pregnancy such as is observed occasionally in humans.

A decrease in the blood sugar level before parturition is also observed in normal subjects, but the drop is not so marked as in the diabetic animals. One possible explanation of the phenomenon may be that the permeability of the placenta increases immediately prior to delivery, thus making it possible for insulin to pass from the fetus to the mother.

The writer's experiments have shown that treatment with insulin is definitely of value for achieving full-term pregnancy. In a long series of experiments without insulin administration, abortion occurred soon after pancreatectomy and full-term pregnancy was achieved in only one rat. When insulin was given the results were more favorable; however, the size of the dose would seem to be of no particular significance.

The birth weights of the offspring of diabetic rats for the most part fall within the standard deviation of the control series. On the other hand, in 3 rats there is a clear increase in weight of offspring. This increase is by more than 50 per cent over the normal mean value for the breed of rat used. These weights fall outside the standard deviation of the normal value, and thus are statistically significant. The mother rats with alloxan diabetes had no enlarged offspring.

According to one view, the cause of giant growth in the children of some diabetic mothers is hyperglycemia in the mother, possibly in conjunction with an increase in the supply of insulin to the fetus. Of the author's 3 rats producing giant offspring 2 had high blood sugar values, but in one case the values were only slightly raised at intervals.

In one of the cases of giant offspring the exact time of conception is known and the pregnancy was not prolonged. Nor is any prolongation of pregnancy likely in the other 2 cases. The author has made a number of experiments with prolongation of the period of pregnancy in rats by means of injections of gonadotropin or progesterone. The weights in these cases do not, by any means, reach those of the giant offspring.

The giant growth has also been associated with the hypophysis. A qualitative and quantitative histologic examination of the hypophysis of the offspring in this material is now in progress. If the volume of the hypophysis is calculated

per gram of body weight, no marked difference can be recognized between the controls and the giant offspring. The giant offspring show a tendency to a decrease in the size of the anterior lobe, and an increase in the posterior lobe, whereas the midlobe remains constant. The histologic picture shows significant differences between the offspring of the control animals and the giant offspring. The anterior lobe of the hypophysis in the controls appears more immature, with cells fairly poor in cytoplasm and with compact nuclei rich in chromatin. The hypophysis of the giant offspring shows greater vascularization and hyperemia. The cells are larger and richer in cytoplasm, with distinct nucleoli. Fetal cell types are much less frequent than in the controls. Thus, definite changes in the cell pattern of the hypophysis are demonstrable in the giant offspring. To what extent these changes may be associated with the giant growth is at present difficult to say. 3 figures.

(If these studies can be extended and confirmed, they promise contributions to our knowledge of diabetes in pregnancy of the highest order. Of especial importance are the pituitary findings. Even casual examination of a giant baby of a diabetic mother will make it plain that the baby is not merely fat but is large in every respect with macrosomia of the important organs. This certainly suggests a pituitary etiology rather than hyperglycemia. —Ed.)

HYPEREMESIS GRAVIDARUM

GLORIA JANG

Bowman Gray School of Medicine, Wake Forrest College, Winston-Salem, N. C.

J. Bowman Gray School Med., 6: 170-179, (Sept.) 1948

The author discusses the etiology of hyperemesis gravidarum, the administration of adrenal cortex extract and the use of vitamins B1, B6, and C as adjuvants to the therapy of this disease.

The adrenal cortical theory was first advanced by Kemp in 1932. He cited the fact that the rise and fall in the production of chorionic gonadotrophin paralleled the duration of nausea in pregnancy. He pointed out that the adrenal cortex undergoes hypertrophy in the first trimester of pregnancy, presumably for the purpose of secreting extra cortin necessary for hepatic detoxication of the excessive quantity of gonadotrophin. Extremely high quantities may result in a cortico-adrenal insufficiency such as that found in Addison's disease, the first signs of which are nausea and morning sickness, regardless of sex. Since normal cortical-adrenal function depends upon at least 2 vitamins, cevitic and pantothenic acids, the increased vomiting creates a vicious circle of cortical-adrenal and vitamin deficiency. Kemp recommended a therapy technique involving the use of 3 to 5 gr. of desiccated adrenal cortex, 5 gr. of calcium pantothenate, and lemon, orange, or tomato juice at bedtime and before arising. Breakfast should be light and all meals should be preceded by a glass of fruit juice.

In 1937, Freeman and Melick treated 15 patients with adrenal cortex extract, body fluids and vitamins, and reported 98 per cent control. Koltz and Kaufman studied the effect of adrenal cortex given subcutaneously and orally and felt that most of their 50 patients were benefited. Studies made by Hughes upon the various glands in true cases of hyperemesis gravidarum revealed hemorrhage and necrosis in the adrenal cortex, changes in the liver, thyroid and kidneys, lending support to the concept that whatever alters the metabolism is toxic and has a damaging effect upon the endocrine system.

Any treatment of this disease is difficult to evaluate as the condition will usually clear up in the first trimester of pregnancy no matter what is done. The important psychic factor is hard to evaluate also, although effort has been made by Kemp and others to control it. However at the present time supervised cortex therapy is of some value and it is by far the easiest and least expensive type of therapy.

The evidence of the etiologic role of chorionic gonadotrophin is not conclusive. The growth of the corpus luteum, the excretion of pregnanediol and the 3 estrogens also parallel nausea and vomiting in pregnancy.

The use of adrenal cortex extract has been shown to be insufficient alone. Insulin, intravenous fluids and vitamin concentrates must be used in severe cases. Vitamin C has been shown to be present in large quantities in the adrenal cortex. Vitamin B1 may be necessary for the normal function of the pituitary and a deficiency in the pregnant woman produces symptoms of toxemia including nausea and vomiting. B1 and B6 have been used together as a means of therapy. Silbernagel reports the relief of 38 out of 40 patients treated with pyridoxine alone. He ascribed the nausea and vomiting to hepatic glycogen deficiency with its resultant ketosis brought on by failure to retain ingested food.

The critical and controlled report of Hesseltine on the value of pyridoxine describes the use of sterile water injections and placebo tablets in a control group. Three of 5 patients in this group were relieved of nausea, while of 11 patients receiving pyridoxine in a similar form, 3 had good results, 3 had fair results and 5 had poor results. Hesseltine concluded that pyridoxine at present is of no more value than other preparations.

Antagonistic evidence makes it impossible to draw conclusions as to the etiology of hyperemesis gravidarum. Vitamins B1, B6, and C are important adjuncts of therapy and suprarenal cortex therapy is more effective and simpler than many other types.

PATHOLOGY OF LABOR AND PUERPERIUM

DESULTORY LABOR AND SEDATION

W. STOLL, S. A. COSGROVE AND P. O. HALL

Bull. Margaret Hague Mat. Hosp., 1: 87-89 (Sept.) 1948

The case is cited of a 28-year-old woman of Italian descent, gravida I, para 0, who was admitted in the 44th week of pregnancy with mild uterine contractions every 15 to 20 minutes. The cervix was thick and one finger dilated, the membranes intact and the vertex presenting and floating. Four hours after admission, moderate to strong contractions were occurring every 2 to 3 minutes, the head was dipping to minus 2 station and the cervix was $1\frac{1}{2}$ fingers dilated. Because of her complaint of severe pain, she was given 100 mgm. of demerol and 0.43 mgm. of scopolamine. Following this sedation, her pains slacked off and never became strong again.

Ten hours after sedation she had made no progress and pelvic x-ray examinations showed an android inlet, a true conjugate of 12 cm., a rather straight sacrum and an adequate midpelvis and outlet. The baby was estimated to be somewhat larger than average. After 32 hours of desultory labor, the membranes were artificially ruptured. During the next 6 hours mild to moderate contractions occurred, with little progress. A low cervical section was done for cephalopelvic disproportion.

This case was brought up for discussion because of the possibility that the sedation may have impaired the quality of the labor. Dr. Stoll quotes Cosgrove on the importance of pain relief in the first stage of labor as conserving the strength and well-being of the mother and, if used judiciously, not injuring the baby.

Dr. Cosgrove states that while recognizing that early sedation may impair the quality of labor, he does not think that the single dose of opiate given this patient made any significant impression on the labor.

Dr. Hall feels that labor can be noticeably impaired by the early exhibition of sedation. It depends a good deal on whether one is making a strenuous effort to maintain a low incidence of cesarean section. Dr. Hall's point of difference is in accepting the patient's own estimate of the pain.

Dr. Cosgrove states that there is found, especially in primiparas, a large component of fear in the pain. It would benefit patients if a little more time were taken to appreciate why a particular patient's threshold for pain is low, and to do what were possible during pregnancy to overcome fear. Even after the patient has been in labor for some time, a sympathetic, painstaking, psychologic handling often can go far to alleviate the fear element in pain. If that were done, then her pain, even if it appeared real only to her, deserves relief.

The trouble that is caused by injudicious exploitation of pain-relief by the lay

press is discussed. Such publications make it hard to get women to regard the matter from an intelligent standpoint. The longer the patient can hold off, the shorter her labor will be and the better off her baby will be. The duty of meeting the psychologic needs of patients is further stressed.

(Case reports presented at informal staff meetings, such as the above, with discussions appended, are sometimes of the utmost value because they not infrequently touch upon those "little" practical questions which are the daily concern of us all but which for some reason or another, are rarely discussed at the larger medical meetings. Yes, as Cosgrove implies, it may well be that this patient would have shown the same desultory type of labor had sedation been withheld; on the other hand, I am certain that the premature use of sedation as well as the premature use of caudal and saddle block anesthesia constitutes, the country over, one of the commonest causes of uterine inertia. All these measures can be counted upon in most cases to retard labor more or less and if the pains are weak, may stop it altogether; moreover, once the mechanism is stopped, it is sometimes difficult to reestablish even after the pharmacologic effect of the drug has worn off. We have had our share of cases like this and time and again we have been distressed to find on retrospect that the pains were good until sedation was given and thereafter were never efficacious. These remarks must not, of course, be taken as a diatribe against analgesic drugs, which are most valuable when used judiciously; but if given too early they occasionally lead to no end of trouble.

It will be noted that the cesarean section was done for "cephalopelvic disproportion." Had the patient been in our hospital we would have said that the operation was done for "uterine inertia." The term "cephalopelvic disproportion," as I see it, is being greatly abused in that it is becoming a waste paper basket for almost all kinds of protracted labor. Most instances of protracted labor are due, not to pelvic factors, but to functional failure of the uterine contractions, that is uterine inertia, as the above case appears to have been. It would lead to clearer thinking, it seems to me, if the dystocia in these cases were charged to faulty powers rather than to lack of pelvic space as the term "cephalopelvic disproportion" implies. We are reluctantly compelled to do quite a few sections for uterine inertia.—Ed.)

CRÉDÉ'S EXPRESSION OF THE PLACENTA

W. F. SHAW

Manchester, England

J. Obst. & Gynaec. Brit. Emp., 55: 502-504 (Aug.) 1948

The writer states that Crédé's method of expression of the placenta is open to much abuse by being used too soon and too vigorously, and that a large percentage of cases of retained placenta are the result of an irregularly contracting uterus produced by the attendant's attempting to save time. The severe shock which sometimes accompanies retention of the placenta seems in many cases to be due to damage from unjustifiable squeezing of the uterus. During a recent examination the candidates stated, with one exception, that they grasped the fundus and squeezed as hard as they could, vigorously pushing down the uterus into the pelvis at the same time.

In support of his interpretation, the author quotes a translation of Credé's original description of the procedure (*Klinische Vorträge über Geburtshülfe* 1853, p. 600):

"... Failing natural discharge of the placenta. . . . In numerous cases, without exception, successful expulsion of the placenta has been obtained within a quarter or half an hour after the birth of the child, by massage through the abdominal wall around the fundus and body of the uterus—gentle at first and gradually increasing in pressure, thus producing an artificially stimulated contraction. When this is at its height I grasped the uterus so that the head lay in the palm of the hand and the fingers and thumb lay along the sides of the organ, exerting a gentle and outward pressure. In each case I felt the placenta slide out of the uterus from under my fingers with such an impetus that it was carried through to the very external genitals; or at least to the lowest parts of the vagina."

The author concluded from this description that Credé meant gentle massage to be used, and this for the purpose only of inducing strong contraction of the uterine muscle, the final squeeze being used only to push the placenta from the lower uterine segment and the vagina. He went on to say that Credé is not strictly entitled to have his name associated with the technique which he described, for John Harvie, in 1767, described a very similar technique for expression of the placenta.

Several members of the Royal Society of Medicine congratulated Sir William Fletcher Shaw on bringing this subject to notice and for presenting its historical aspect. All agreed that squeezing the uterus is conducive to shock and is dangerous if repeated.

(The admonition expressed in this paper comes with the authority of a preeminent leader of our specialty and should do much good. Squeezing the uterus does all the bad things that Sir William imputes to it, and more too, and has no place in modern obstetrics. Under present day conditions, manual removal of the placenta from within is much safer.—Ed.)

THE NEWBORN

NEW CLASSIFICATION AND NOMENCLATURE FOR NEW-BORN INFANTS INCLUDING PREMATURES AND ABORTIONS

ARVO YLPPÖ

Acta paediat. 35: supp. 1, 160-163, 1948

Everyone engaged in clinical or pathological work relating to the care of prematurely born infants knows how impossible it has been so far to compare the material of different pediatric and above all obstetric clinics. In some quarters the infants are still being classified according to their length at birth, no definite length having been agreed upon, however, 45, 47, even 48 cm. being regarded as boundary lines for premature births. In another connection the author has tried to prove that there is no advantage in going by length rather than by weight. Further, he has been able to demonstrate that the same nurse or midwife may attain different results, varying up to 10 per cent, in measuring the length of a child on successive occasions.

Yet, the author's proposal that 2500 grams should be adopted as a distinguishing limit between prematures and full-term infants has also been advocated and even applied by many authorities. This distinction was officially adopted in 1935 by the American Academy of Pediatrics, and the Royal College of Physicians of London and the Royal College of Obstetricians and Gynecologists of England have also expressed agreement with his view.

But where should the lower boundary line for prematures be drawn? How shall prematures be distinguished from abortions? To pediatricians the question seems a simple one. They draw the line as low down as possible, as children weighing 500-600 grams at birth have been known to live for shorter or longer periods.

Obstetricians, however, regard the matter differently. In their textbooks it is stated, as a rule, that if the pregnancy is interrupted before the 28th week the fetus cannot survive and that such cases should be regarded as abortions. As it is commonly admitted that it is often impossible to determine with certainty the duration of the pregnancy, one has tried to base the distinction on the length of the child, and 32 cm. (sometimes even 35 cm.) has been suggested as a distinguishing value between prematures and abortions. In Sweden, for instance, all stillborn fetuses measuring up to 35 cm. are regarded as abortions, while all fetuses weighing less than 2500 grams, but having breathed and shown signs of life, are regarded as prematures, as also all stillborn fetuses measuring from 35 to 47 cm.

In the author's country, Numers, trying to determine the mean weight of fetuses aged 28 weeks, which age is "popularly" and in the textbooks regarded as

being the upper limit of abortions, has fixed the mean weight of fetuses aged 29 weeks at 1250 grams.

This coincides with the weight advocated by Henderson (J. Obst. & Gynaec. Brit. Emp.) last year as being the most suitable lower limit for prematures. For smaller fetuses he suggests the denomination "præviabiles."

Numers' results, derived from Parviainen's considerable Finnish data, show that the mortality of children weighing between 600 and 900 grams at birth is 100 per cent in the first year, and of children weighing 900-1400 grams, 97.2 per cent.

As the number of survivals among the children weighing less than 1250 grams at birth was so small in his material, Numers arrived at the conclusion that the limit between prematures and abortions should be fixed at 1250 grams which would also tally with the prevalent "popular" and textbook notion, according to which a fetus less than 28 weeks old is an abortion.

(As the author indicates, his proposal some years ago that 2500 grams be adopted as a borderline between premature and mature infants, has been generally adopted and may be regarded as more or less standard. The rationale of this figure lies in the fact that infants of this size (but not smaller infants in the white race at least) stand on the average just as good a chance of survival as do infants of 3000 or 3300 grams, let us say.

In regard to the lower limit of prematurity, the problem here resolves itself in establishing a similar borderline at the other extreme between premature infants and nonviable conceptuses or abortions. The issue here, by definition, is simply and clearly ability to survive. Now a case has been reported in which an infant weighing only 14 ounces or 397 grams on the 2nd day of postnatal life, survived and weighed at 1 year, 13 pounds 12 ounces or 6238 grams (Canad. M. A. J. 40: 69, 1939). It may be assumed that this infant weighed over 400 grams at birth. Because this baby weighing slightly over 400 grams did survive, it must be conceded, strictly speaking, that an infant weighing over 400 grams *can* survive although everyone realizes that the likelihood of its doing so is infinitesimally small. This presumably is the rationale of the 400 gram borderline used by Potter and Adair. On this basis the range of prematurity would be between 400 and 2500 grams and for the reporting of overall prematurity statistics, this is probably as defensible a classification as can be established.

However, as everyone knows, the survival of an infant weighing less than 800 grams is nothing short of a miracle and hence the numerous attempts to divide the premature group into 2 subdivisions: those infants in which there is no appreciable likelihood and those in which there is an appreciable chance of survival. Here we get into trouble. In the first place, with improving pediatric care this figure has moved downwards and is continuing to do so. In the second place, terminology is difficult, if not meaningless. Thus the term "previable" for the smaller group demands the occasional inconsistency that a "previable" infant has survived. For these reasons it would seem desirable in my opinion to abandon these attempts at subdivision of prematurity by name and simply report total figures, that is, 400 to 2500 grams, plus subdivisions by weight without any implication in regard to viability, that is, 400 to 999 grams; 1000 to 1499 grams, etc. Or by 250 gram groups if it is deemed desirable.

As Ylppö states, the 28 week borderline is deeply entrenched in the lay mind and in legal definitions and it would be desirable to have a weight figure in our classification corresponding to this. However, the most authoritative American figures which are available to me at the moment give a weight figure for a 28 week fetus much nearer to 1000 grams than the 1250 gram figure recommended in the above article (Streeter, 1045 grams; Scammons and Calkins, 971.4 grams).

In view of its great importance in comparative studies of premature mortality, this might be a suitable topic for consideration at the coming Congress of Obstetrics and Gynecology, —especially if Dr. Ylppö, the preeminent authority in this field, could be persuaded to take part.—Ed.)

ERYTHROBLASTOSIS FETALIS TREATED BY REPLACEMENT TRANSFUSION VIA THE UMBILICAL VEIN

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Am. J. Dis. Child., 75: 457-461 (Mar.) 1948

Originally, the treatment of erythroblastosis fetalis consisted merely of transfusion of whole blood as needed for developing anemia. Usually, the father's blood, Rh positive, was used; the mortality was then about 40 per cent. After recognition of the Rh factor in 1941, it was logical to change to transfusion with only Rh negative blood. Gross mortality figures now showed about 30 per cent deaths. Evidence accumulated by the author's laboratory and by many others proved that Rh positive cells given to newborns with severe hemolytic disease are destroyed faster, produce more jaundice and, occasionally, cause collapse of the patient. Four such cases have been seen by the writer.

Since many infants with erythroblastosis are severely affected at birth, or even stillborn, it seemed logical to introduce one further step in modifying the disease. This consisted of delivery 2 to 3 weeks before term in women with a demonstrably high or increasing titer of anti-Rh agglutinins, especially when they had lost previous children from the disease. This further reduced the mortality rate to 20 per cent.

Finally, since some of the infants born alive to mothers having much Rh antibody looked well for 24 hours or more but then suddenly became sick, it seemed necessary to do something further. By routine tests it was found that most such ill children had appreciable amounts of passively transferred antibodies in their cord or peripheral blood serum at birth and a preponderance of bound or "blocked" red cells. Therefore, replacement transfusions seemed indicated.

The author's first few patients so treated offered considerable difficulties. The longitudinal sinus may not be readily located shortly after birth because of molding of the head. Peripheral veins and arteries are difficult to enter without careful dissection by experts. Heparinization to prevent clogging may be dangerous at this period of life. Exposure of the newborn infant to 2 hours of surgical manipulation may be a shocking procedure.

Thin-walled plastic catheters were obtained which are made of polyvinyl and are flexible and nonirritating to nerve and vascular tissues. The umbilical vein lends itself to easy passage of such catheters for the first 12 hours or more of life.

The patients to be treated by replacement transfusion are selected on the basis

f (a) visible clinical manifestations of hemolytic disease at birth or shortly thereafter, and if no such signs occur, on the basis of (b) laboratory tests proving that the mother has an important amount of Rh antibody or that her infant has Rh positive cells, free antibody in its circulation and/or bound cells.

The method of treatment is illustrated by lantern slides. The infant should be kept warm. A Hess bed is the recommended operating table. The airway must be cleared and suction used on the larynx and throat as needed. Oxygen is administered constantly. The blood for transfusion should be compatible, Rh negative or group O in type and neutralized with A and B substances.

Test samples are taken 3 or 4 times during the process of removing the infant's blood. Five hundred to 1,000 cc. of blood is used for the transfusion. At the end of the operation, 6 to 10 cc. of 10 per cent solution of calcium chloride is injected intravenously. Penicillin and sulfadiazine are given prophylactically for 48 hours, and the infant is fed cautiously and not too early.

In the author's first 50 cases the mortality has been about 10 per cent. About 8 individual cases have been truly dramatic. All but 3 of the infants were discharged home with the mother. The incidence of kernicterus has not seemed to be affected.

The writer points out the need for good judgment and careful pediatric supervision of infants with erythroblastosis fetalis. The present mode of treatment offers an improvement in the technic and simplicity of replacement transfusion rather than a panacea for all erythroblastotic babies.

INTERPRETATION OF RH ANTIBODIES

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Am. J. Clin. Path., 18: 690-699 (Sept.) 1948

This paper deals with the interpretation of Rh antibodies in maternal serum and is based on a study of the antibodies in 182 mothers of erythroblastotic babies. Wiener was the first to attempt a correlation between the various forms of Rh antibodies in pregnant women and the clinical manifestations in erythroblastotic infants. He stated that "bivalent" (for which the senior author suggests the term, saline) agglutinins are mainly responsible for icterus gravis, and that the so-called congenitins and blocking antibodies are responsible for the severe damage leading to hydrops and intrauterine death. In this series, agglutinins alone were found in 64 per cent of mothers whose babies had icterus gravis, whereas blockers and congenitins were present in only 14 per cent of such mothers. Only 8 per cent of mothers of stillborn babies were found to have saline agglutinins, whereas 43.9 per cent had congenitins and blockers.

In the total of 182 cases forming the present series, 40.1 per cent had blocking

antibodies in the maternal serum, while 59.9 per cent did not have them. In a group which includes mothers of all deceased infants, the incidence of blocking antibodies does not differ significantly from the incidence in the whole series.

When the deaths are divided into 2 groups, (a) those due to stillbirth or hydrops, and (b) those due to other causes, a significant difference appears. In mothers of the first group, the incidence of blocking antibodies is increased as compared with the incidence of those antibodies in the whole series, the difference in percentages, 28.4, being more than 5 times the probable error of ± 5.2 . In mothers of the second group, saline agglutinins predominated as compared with the whole series, the difference in percentages, 15.6, being more than 3 times the probable error of ± 4.9 .

In mothers of infants that survived, saline agglutinins were somewhat more frequent than in the whole series, the difference in percentages, 9.7, being more than twice the probable error of ± 4.3 .

In the presence of icterus gravis, saline agglutinins occurred in more than $\frac{1}{4}$ of the mothers, and the difference in percentages, 16.7, was greater than 4 times the probable error of ± 3.8 . Finally, the most significant difference was exhibited in the group of mothers who had received transfusions prior to birth of the affected child. More than $\frac{4}{5}$ of this group had blocking antibodies and the difference in percentages, 42.8, was more than 8 times the probable error of ± 5.2 .

In 73 mothers blocking antibodies were present; in 109 mothers they were not. Each of these groups was then subdivided into 3 classes according to the clinical condition of the infant: stillborn infants or infants with hydrops, infants with icterus gravis, and infants with hemolytic anemia. In the presence of blocking antibodies in the maternal serum, the chances for the birth of an infant with hydrops or who is stillborn are about even, while the chance for an infant with icterus gravis is about 1 in 3. The absence of blocking antibodies in the maternal serum gives a chance for the occurrence of stillbirth or hydrops of about 1 in 6, while 75 per cent of the infants developed icterus gravis.

The difference in occurrence of stillborn or hydropic infants in mothers with blocking antibodies as compared with those without blocking antibodies is significant, being more than 7 times the probable error. The difference in occurrence of icterus gravis in mothers without blocking antibodies as compared with those with blocking antibodies is also highly significant, being more than 8 times the probable error.

In 74 of the present group of cases, in which antibodies could be studied before delivery, a study was made of the relation between the maternal titer of serum albumin agglutinins and fetal mortality. In those mothers with a titer of 1:10 or less, about $\frac{1}{3}$ of the children died and $\frac{2}{3}$ survived, while in those mothers with a titer higher than 1:10, the proportions of deaths and survivals were reversed. The difference between the death and survival rates in the 2 groups, 33.3 per cent, is statistically significant, being more than 4 times the probable error of ± 7.8 . The presence of blocking antibodies adds an additional aggravating factor which may be lethal. Thus, high antibody titers and presence of blocking antibodies, occurring singly or together, seem to lower the chance of survival of the infant

The death rate was found highest when both factors were present, and the survival rate was highest when both factors were absent.

It is possible that the significance of blocking antibodies is different in women with a history of transfusion than in those without such a history. In women with a history of transfusion, the presence of blocking antibodies appears in the authors' material to be less ominous for the fate of the child, than in those having blocking antibodies but no history of a transfusion. It is emphasized, however, that the differences are at the border of statistical significance. 1 figure.

THE VALUE OF THE COOMBS TEST IN DETECTION OF ISO-SENSITIZATION OF THE NEWBORN

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M. J. Australia, 2: 143-150 (Aug. 7) 1948

A new method of testing for "incomplete" or "blocking" Rh antibodies and for weak Rh agglutinins was described in 1945 by Coombs, Mourant and Race who found that rabbit anti-human globulin serum would agglutinate red blood cells which had absorbed Rh antibodies onto their surfaces either in vivo or in vitro. This factor was applied in the development of two tests for detecting such antibodies which are known as the "direct Coombs test" and the "indirect Coombs test." In the direct test, cells suspected of having been sensitized are exposed to the action of immune rabbit serum, which will agglutinate them if they have previously absorbed antibodies. In the indirect test, serum suspected of containing antibodies is mixed with normal cells, which are subsequently tested with immune rabbit serum. The direct test is more commonly used but it has the disadvantage of being not completely specific. The indirect test is very sensitive and detects weak concentrations of Rh antibodies.

The authors have performed 1580 direct tests on cord blood, 32 of which gave a positive reaction. In 5 of the 32 positive tests the mother and child were Rh and ABO compatible, in 22 they were Rh incompatible and ABO compatible, in 3 they were Rh compatible and ABO incompatible, and in 2 cases the mother and child were incompatible in both ABO and Rh factors. It was felt that the "direct Coombs test" was slightly more sensitive than other methods in detecting Rh immunization, although occasional positive reactions are observed in the absence of any clinical or other serological evidence of immunization. These false positives are probably the result of sensitization of the red cell by an antibody capable of reacting with the rabbit antihuman serum. The result of the direct test was only occasionally positive in cases of ABO incompatibility between

mother and child. In 2 of the 3 cases of this kind in this series there was also jaundice, anemia, or both in combination. A positive result to the Coombs test should therefore give warning of the possible development of clinical manifestations of hemolytic activity. The prediction that an infant is unlikely to develop erythroblastosis can be made on the first day of its life if the result of the direct Coombs test is negative, in spite of the presence of Rh antibodies in the serum of its mother.

In certain cases errors in the determination of the type of Rh factor may be clarified by the Coombs tests. The direct Coombs test may reveal that the apparent Rh negative status of the newborn infant's blood is due to coating of the infant's cells with Rh "blocking" antibodies. Occasionally, if the erythroblastotic infant's blood is taken after a transfusion with Rh negative blood, a negative reaction will be obtained by the direct Coombs test, but the indirect test will demonstrate that the infant is Rh positive. This illustrates the usefulness of the indirect test in confirming the presence of small concentrations of antibodies in the infant's serum. The authors have examined the serum of 48 mothers and have found the indirect test as reliable as other tests now in vogue.

REPLACEMENT TRANSFUSION IN ERYTHROBLASTOSIS FETALIS (REPORT OF 24 CASES)

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Canad. M. A. J., 59: 378-379 (Oct.) 1948

The writers point out that in erythroblastosis, removal of the child's blood and replacement with Rh negative blood would appear to be the ideal form of treatment, inasmuch as one might remove deleterious isoagglutinins and at the same time replace oxygen-poor erythroblasts with mature red cells. Replacement transfusion is not a new procedure and it was in use as early as 1925 in the treatment of erythroblastosis.

Twenty-four cases have been treated by this procedure at the Hospital for Sick Children. The replacement was carried out by placing a woven venous cannula in the umbilical vein; 20 cc. of blood was withdrawn from the vena cava and immediately replaced with 20 cc. of fresh Rh negative blood, allowing 5 minutes for the removal and insertion of each 20 cc. This was repeated until 100 cc. per pound of body weight had been replaced, leaving a positive balance of 15 cc. per pound. To prevent clotting, $\frac{1}{2}$ cc. of a 1:100 solution of heparin in saline was used in 20 cc. of blood, and clotting time was determined at frequent intervals during the procedure. The appearance of a murmur and undue acceleration or slowing of the heart beat were indications to proceed more slowly, acute cardiac embarrassment being one of the most serious complications to the procedure.

Analysis of the 24 cases showed the average birth weight to be 6 pounds, 3 ounces, and the age on admission ranged from one hour to 4 days. Jaundice was present in 22 cases and an enlarged liver or spleen was present in 21 cases. The hemoglobin ranged from 4.2 to 16.2 gm., with an average of 9.8 gm. The red blood count varied between 1.1 to 5.3 million. All of the infants were Rh negative and antibodies were demonstrated in 20 of the infants. All of the mothers were Rh negative and all of them had demonstrable antibodies. Fourteen of the mothers had a history of previous miscarriages or stillbirths and 3 of them had had previous transfusions. The average amount of blood removed from the infant was 440 cc. and the average amount replaced was 480 cc. There were 5 cases of cardiac embarrassment encountered with one death. There were 2 other deaths in the series, one on the twentieth day due to intestinal intoxication and one due to erythroblastosis. The average stay in the hospital was 12 days.

The authors conclude that replacement transfusion has given the best results to date in the treatment of erythroblastosis fetalis. 1 figure.

THE VERNIX CASEOSA AND SUBNORMAL TEMPERATURE IN PREMATURE INFANTS

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J. Obst. & Gynaec. Brit Emp., 55: 442-444 (Aug.) 1948

In spite of modern methods of nursing and incubation, including various forms of treatment, the problem of persistent subnormal temperature in the premature infant still remains to be completely solved. The question arises as to whether, in the majority of cases, the subnormal temperature is due to dysfunction of a poorly developed thermal center, to a subnormal metabolism, to abnormal heat loss, or to a combination of these factors. The present study was concerned with prevention of abnormal heat loss.

An experiment was made in which the vernix was not removed but was allowed to separate in the natural way. This usually occurred by the fifth day, except in the folds of the body, where separation was not completed until the tenth day. After the natural separation of the vernix there was little, if any, of the superficial hyperemia invariably present following its forcible removal. A study of the results of this technique has shown a considerable reduction in the number of cases of subnormal temperature. Of 122 cases seen prior to 1940, in which the vernix was removed, 38 showed subnormal temperatures, while of 90 cases observed since 1940, in which the vernix was allowed to separate naturally, only 6 showed subnormal temperatures.

The author concludes that in addition to being a protective covering to the

skin, the vernix may influence heat control, especially in the premature infant. The vernix caseosa has also been proved to contain substances which may be of value to the infant, notably estrogen, and removal of the vernix may deprive the infant of valuable intrinsic substances. In the premature, removal of the vernix also exposes the poorly keratinized skin to bacteria, and since the present policy has been in force, the author has noticed a significant drop in infections in these infants.

SOCIAL AND LEGAL ASPECTS

ABORTION AS A CAUSE OF DEATH

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Am. J. Pub. Health, 38: 1434-1441 (Oct.) 1948

Abortion affects population growth in 3 ways: (1) In each case by terminating the current pregnancy before the fetus has reached viability; (2) In some cases by making the women sterile and thus preventing further pregnancies; (3) By causing the death of a certain number of women. The present study was devoted to the third aspect only. Deaths from septic and nonseptic abortions were considered separately because of the close association of illegal induction and fatal infection. The data were presented in terms of annual mortality rates per million women of reproductive age.

The overall tendency has been definitely downward in the last 30 years, and in the United States the rate has fallen from 99 septic and 37 nonseptic in 1927-28 to 18 septic and 9 nonseptic in 1945. The decreased rate has occurred primarily in white women, and abortions of both types are nearly 4 times as common in the colored female. When regions of the United States are analyzed, the highest mortality rate for septic abortion occurs in the northeast states, while the highest rate for nonseptic abortion deaths is found in the southern states. Septic abortions with maternal death are more common in urban areas in the white race, while in the colored race the rate is higher in small urban and rural areas of the south.

Studies of the mortality rates in England, Prussia and Germany revealed similar declines in recent years. The most rapid decline in Germany occurred during the years 1933-38, at the time of the population drives. England also showed a rapid decline in the thirties, but at present the rates for both septic and nonseptic deaths are almost identical with the rates in the United States.

BIRTH, INFANT DEATH AND STILLBIRTH DATA,
WISCONSIN, 1947

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Wisconsin M. J., 47: 870-874 (Sept.) 1948

In Wisconsin in 1947 there were 83,907 live births, 1410 stillbirths and 2470 infant deaths. Over the 10-year period from 1937 to 1947 there was a decrease from 43.5 infant deaths per 1000 live births to 29.4 deaths, and the stillbirth rate was 16.8 in 1947 as compared to 23.4 a decade earlier. The percentage of premature births increased slightly. The rate of total deaths occurring before the end of the first year of life has risen to 75.7. The most common causes of infant death were prematurity, congenital malformations and birth injuries, with these 3 conditions making up 60 per cent of the deaths within the first year.

The effects of prenatal care, parity, age of the mother and color were analyzed as to relationship to stillbirth and infant mortality rates. In the stillbirth group, a lower portion of the mothers sought care early in pregnancy and a relatively higher proportion were associated with the first pregnancy. It was found that the same relative proportion of live births and stillbirths occurred to women under 20; however, the number of infant deaths to mothers in this age group was slightly higher than in other age groups. The highest rate of stillbirths occurred in the age group from 20 to 34 years. In this series color did not appreciably alter the stillbirth and infant mortality rates.

Pregnancy experience showed that only 7.7 per cent of the mothers delivered of liveborn children had prenatal complications. This increased to 23.4 per cent among the cases of infant death and to 39.9 per cent among the cases of stillbirth. Complications of labor occurred in 11.9 per cent of live births, in 22.1 per cent of infant deaths, and in 38.2 per cent of stillbirths. The most common complications of pregnancy were toxemia, bleeding, renal disease, threatened abortion, multiple births, anemia and premature rupture. The most common complications of labor were prolonged labor, abnormal presentation, breech, hemorrhage, disproportion, retained placenta, cord complications and eclampsia.

The author points out that improvement in infant mortality and stillbirth rates has been made and that further steps can be taken through analysis of large series of cases. Proper filing of stillbirth and infant mortality data by the attending physician is of major importance.

MISCELLANEOUS

OBSTETRICAL SERVICE IN INDIA

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J. Am. M. Women's Ass., 3: 411-412 (Oct.) 1948

Ninty-five per cent of India's babies are born at home and about 40 per cent are attended by trained personnel, either doctor or nurse-midwife; the rest are attended by a "dais" which means a "helper." The dais originally aided a natural process but of late she has begun to interfere with methods of her own, and childbearing has become more dangerous.

Pregnancy and childbirth are considered natural and to have a normal ending. Factors playing a part in this attitude are the youth of the pregnant women, the greatest fertility rate is between the ages of 14 and 15, and the mode of life which requires vigorous daily exercise.

Sepsis is controlled by the practise of setting aside a confinement room which no one is allowed to enter for the first 8 to 10 days after the delivery. This also allows for an undisturbed relationship between mother and child.

The greatest problem today, as industrialization increases bringing with it malnutrition and disease, lies in improving the diet of the pregnant woman and improving general health conditions. The diet of the parturient woman traditionally consists of almond in milk. But poverty has limited the number who can even afford milk as a basic food. There seems to be a correlation between the nutrition of a province and the degree of obstetrical complications. About 3 per cent of the deliveries become complicated enough to require hospitalization.

The second problem in obstetrics is that of training personnel. In the large cities where there are well-equipped hospitals, 80 per cent of the deliveries take place in the hospitals now but there is a great need for the woman obstetrician or the trained dais in the rural areas as the Indian woman prefers to be cared for by one of her own sex. Laws against midwifery are present but cannot be enforced until there are sufficient numbers of trained personnel. Therefore, a program has been set up to give training to the dais for a 6 months' period. After this, she is taken into the public health service and allowed to practise in a rural area under the supervision of a district doctor or nurse-midwife. This method has been successful.

Maternity-child health centers have progressed and are now administered by the province governments.

OPERATIVE OBSTETRICS

A SURVEY OF CESAREAN SECTION IN MINNEAPOLIS, MINNESOTA, IN 1946

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Minnesota Med., 31: 987-989 (Sept.) 1948

This study was made in order to compare the results of cesarean section in this community with those in other localities. For comparison, a 5-year study of cesarean section in Ramsay County, Minnesota, was used. This latter study was made by Skinner, and covered the period from 1937 through 1942. During this period there were 28,868 hospital deliveries with 434 cesarean sections, an incidence of 1.5 per cent. There were 8 maternal mortalities (1.84 per cent) and a fetal mortality of 11.2 per cent.

Of the 15,556 recorded deliveries in Minneapolis in 1946, 405 were by cesarean section, an incidence of 2.6 per cent. Only 2 maternal mortalities occurred. In addition, one postmortem cesarean section was performed. Infant deaths numbered 16 (3.9 per cent) or 41.1 per 1,000 live births, compared to an over-all infant death record in the city of 27.8 per 1,000 live births.

A comparison of cesarean sections in Minneapolis with those recently reported from other communities and with those in the Ramsay County study shows that the trends seem parallel, namely, a slight increase in the incidence of the procedure with a reduction of maternal and fetal mortality.

Of the 405 cesarean sections performed in 1946, 240 were of the classical type, while 156 were low cervical sections. Seven cesarean hysterectomies were performed, an incidence of 1.7 per cent. There was one vaginal cesarean section and one abdominal pregnancy. The morbidity with the classical operation was 28 per cent; with low cervical sections, 21 per cent; and with cesarean hysterectomy, 28.5 per cent.

A study of classical and low cervical section in regard to morbidity in relationship to length of labor and condition of the membranes showed that the low cervical operation may seem to have an advantage in all conditions except when the patient is not in labor and has intact membranes.

Cyclopropane with other inhalants appeared to be the prevailing choice of anesthesia, with local infiltration plus additions next. There was no evidence of advantage from the standpoint of morbidity in the type of anesthesia used.

Cesarean section in Minneapolis, as revealed by this study, shows a higher maternal and infant mortality in comparison to normal delivery during the same period. However, it must be concluded that cesarean section is done for relatively definite indications that jeopardize the life of the mother or baby, a situation that cannot be analyzed statistically when related to normal vaginal delivery.

(Statistics from various sources would seem to indicate that the incidence of cesarean section in the country at large is about 2 per cent of all deliveries or slightly less. It is naturally higher in the metropolitan centers because many complicated cases from rural districts are sent there for management and because of other factors. Thus, in the above study, the frequency of abdominal delivery in Minneapolis was 2.6 per cent, but was decidedly lower in Ramsay County.

Through the courtesy of Dr. Buford Word of Birmingham, Alabama, and Mr. Ralph W. Roberts, State Registrar, Montgomery, Alabama, the following figures have been put at my disposal. In 242,438 total births which occurred in Alabama during the 3-year period, 1945-1947, there were 3205 cesarean sections, an incidence of 1.32 per cent. Of these total deliveries, slightly under one-half took place in hospitals so that the incidence of abdominal delivery in hospital obstetrics was 2.29 per cent.

The present day mortality figures reported for cesarean section continue to be a source of amazement as well as gratification to anyone acquainted with comparable statistics of but a decade ago. In the 405 abdominal deliveries reported by Ehrenberg in Minneapolis, there were only 2 maternal deaths, a rate of 0.5 per cent. Of more statistical significance, because of their greater size, are the Alabama statistics. In the 3205 cesarean sections performed there between 1945 and 1947, there were only 31 maternal deaths, a mortality incidence of 0.91 per cent. It is informative to note that 11 of the deaths occurred in association with eclampsia. During this same interval of time there were 669 maternal fatalities from all causes so that the cesarean section deaths made up but 4.6 per cent of the total obstetric mortality. In view of the large colored population of Alabama, this cesarean section record would seem in general to be a most creditable one,—indeed, almost as good as the Minneapolis report.—Ed.)

CYCLOPROPANE IN CAESAREAN SECTION

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Canad. M. A. J., 59: 464-467 (Nov.) 1948

Very little has been reported in the literature concerning the use of cyclopropane in cesarean section. The anesthetic of choice in this procedure should at all times be under the control of the anesthetist; it should produce good abdominal muscle relaxation and contraction of the bowel, it should provide a maximum oxygen supply, the baby should cry spontaneously immediately after delivery, the uterus should contract well and bleeding should be minimal. The author believes that cyclopropane fits these criteria, and reports his results in 378 cases. Up to 1940, 102 cases were given cyclopropane, then prepared for commencement of the surgical procedure. Since 1940, 276 cases have been given all preparation prior to anesthesia, thus reducing the total time under cyclopropane.

Preoperatively, the mother is given scopolamine, gr. 1/200 and the nose and pharynx are sprayed with a bland oily mist. Following full surgical preparation, including draping of the patient, cyclopropane is administered in a concentration of 40 per cent in oxygen and is maintained at that concentration until the second plane of the third stage of anesthesia is reached. The patient is maintained at a

light second stage until the cord is cut. If the baby does not breathe successfully, the anesthetist is prepared to pass a rubber catheter so that mucus may be aspirated.

Postoperatively, the mother receives pantopon and intravenous fluids or blood as indicated. A complete description of the operative procedure is not felt to be appropriate; however, two points are emphasized. In the interest of rapid delivery of the fetus, bleeding points in the abdominal and uterine walls are temporarily ignored or simply clamped with hemostats. Following delivery of the fetal head from the uterine cavity, 10 units of pitocin are injected into the uterine muscle and 1 cc. (1/320 gr.) of ergotrate is injected intramuscularly.

The great majority of the cesarean sections performed were done because of contracted pelvis, with placenta previa and previous section being the next most common indications. Three hundred and six of the sections were classical, 63 were low, 6 were cesarean hysterectomies, and 3 were classical with a myomectomy. There was one maternal death 2½ days postoperatively in a woman who had a ruptured uterus and a dead fetus. Autopsy showed bronchopneumonia and pulmonary edema. There were 9 fetal deaths, 2 with complete abruptio placentae, 2 with ruptured uterus, and one each with placenta previa and prematurity, congenital absence of the kidneys, toxemia, fetal atelectasis and a large unexplained stillbirth.

The author feels that, combining low toxicity, rapidity of action and high oxygen content, cyclopropane is the ideal agent for cesarean section. In so far as the infant is concerned, spontaneous respiratory activity on delivery was the rule and prematures seemed to do exceedingly well. In so far as the mother is concerned, the smooth postoperative course, freedom from cyanosis, excellent uterine tone and ease in carrying out additional procedures make it the agent of choice. Generally, the use of cyclopropane in cesarean section, in the author's hands, has been highly successful.

(Here is another commendable cesarean section report. Since operations for rupture of the uterus are not usually classified as cesarean sections and since the one death in this series followed surgical intervention for that accident, it can be said that the author has performed 376 consecutive cesarean sections (there was 1 other rupture) without a single maternal death. In the vast majority of these operations, it will be noted, the classical technic was employed.

To turn to the main subject of the article, there is one thing which would seem certain about this problem of analgesia and anesthesia in obstetrics, and that is this: once a man has come to like one or another of the accepted methods, he will usually do well to stay with it. The grass in the other pastures may look more inviting at a distance, it is true, but will usually prove to be no greener. In the exemplary obstetric service of Nicodemus at the Geisinger Memorial Hospital in Danville, Pennsylvania, some 90 per cent of the deliveries are conducted under continuous caudal anesthesia and he and his associates are as happy as they can be about their results. In this same issue of the Survey, Hershenson, an anesthesiologist of great experience, reports his preference for barbiturates and inhalation anesthesia in 80 per cent of cases and is certain that that is the most satisfactory and safest technic. Many clinics have swung to saddle block anesthesia and extol the advantages of that procedure. During the past 8 years we have delivered the great majority of our cases with intravenous sodium pentothal and feel very much at home and safe with that agent. Now comes Brown with his 376 cesarean sections under cyclopropane anesthesia and agrees

with authors such as Karp and Richardson (Surg. Clin. North America 23: 59, 1943) that this is the ideal anesthetic at least for abdominal delivery. Beyond question each of these procedures has its advantage and each—God knows—has its hazards. As I see it, the great desideratum is that every obstetrician have at his disposal at least two of these procedures, one for systemic effects and the other for conduction or local action, and know them backwards and forwards.

Whether judged from an obstetric or an anesthesia viewpoint, Brown's report is an enviable one and he deserves congratulations.—Ed.)

STUDIES ON HYPERTENSION: VII. MECHANISM OF THE FALL IN ARTERIAL PRESSURE PRODUCED BY HIGH SPINAL ANESTHESIA IN PATIENTS WITH ESSENTIAL HYPERTENSION

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Arch. Int. Med., 81: 352-363 (March) 1948

It has been suggested previously by various workers in the field of physiology of hypertension that the fall in blood pressure due to spinal anesthesia is the result of decreased cardiac output, caused by decreased venous pressure and diminished venous return to the heart. Other studies seem to indicate that the drop in blood pressure is due to interruption of vasomotor function. In order to clarify this subject, simultaneous arterial and venous pressures were determined in 5 normotensive subjects. Twelve separate studies were made in 10 patients with a clinical diagnosis of essential hypertension. Control observations were made and similar determinations were then made with high spinal anesthesia induced by 150 mgm. of procaine hydrochloride. Observations were continued during recovery stages. The arterial pressures were determined in the usual manner with the cuff and mercury manometer. The venous pressure was measured with a water manometer and with the needle inserted in the antecubital vein.

In the majority of patients with essential hypertension, the arterial pressure fell before the venous pressure. In one case the venous pressure fell without any significant change in the arterial pressure. In only 2 cases did the venous pressure drop first, and in these 2 cases the arterial pressure fell to its lowest level before the venous pressure reaches its lowest point. Also, the arterial pressure rose again while the venous pressure continued to fall. It was further noted that there was no constant time correlation between the falls of arterial and venous pressures during high spinal anesthesia in patients with hypertensive disease.

It was concluded to be extremely unlikely that decreased venous return and diminished cardiac output are causative in the fall of arterial pressure caused by high spinal anesthesia in either normotensive or hypertensive individuals. It was further felt that these data support the likelihood that the falls in arterial pressure are caused by interruption of vasomotor function. 13 figures.

THE COLD PRESSOR TEST AS A CRITERION FOR THE
SELECTION OF PERIDURAL ANESTHESIA

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Zentralbl. f. Gynäk., 70: 92-97, 1948

In its present form peridural anesthesia has a tendency to produce circulatory collapse. On the other hand its advantages, such as complete relaxation of the abdominal muscles and lack of postoperative pulmonary complications, are manifest. The occurrence of circulatory collapse must in some degree be mediated by the lability of the individual circulation.

The cold pressor test of Hines and Brown appeared applicable for the prognostic evaluation of the circulation prior to peridural anesthesia.

Peridural anesthesia was introduced in 1931 by Dogliotti and is a variation of spinal anesthesia. It possesses the advantages of segmental localization and freedom from side effects, and is reasonably safe if novocaine is employed. Pontocaine, used as a peridural anesthetic, however, frequently leads to circulatory collapse even though it has a greater anesthetic potency than novocaine.

During the past year the author has given 550 peridural anesthetics. During the first 6 months she used 45 cc. of 0.2 per cent pontocaine. During this time she observed several severe cases of vascular collapse and 2 fatal cases of vascular collapse. In the second 6 months she gave only 30 cc. with the same technique.

The cold pressor test was carried out in the following manner. The exact value of the resting blood pressure and pulse was determined. The forearm was then placed in a water bath at 4°C. for one minute. The blood pressure apparatus was placed on the other arm. The blood pressure was measured twice at intervals of 30 seconds and then every 2 minutes until it either returned to normal or until 8 readings were obtained. The pulse was similarly determined. The general physical and psychic makeup of the patients was also assessed.

The normal reaction is an immediate rise of blood pressure of 20 to 50 mm. of mercury. After the forearm is removed from the cold bath the blood pressure rapidly falls to a value on the average of 10 to 20 mm. of mercury below the resting value and then returns to the resting value gradually. If the rise in blood pressure is higher or if the blood pressure does not return to normal after 8 readings, vascular complications are to be expected. Seventy patients were thus tested. Fifteen patients were excluded because, either on technical grounds or because the test results were imperfect, ether anesthesia was thought to be indicated. Of the 55 remaining cases, 44 showed an agreement between the test blood pressure curve and the anesthesia blood pressure curve. In 35 cases both curves were normal. In 5 cases, both curves showed fall of blood pressure values. In 6 cases the result of a test was not unusual and nevertheless the peridural anesthesia caused a severe fall of blood pressure during the operation. In these cases

it was possible that the operation itself might have caused the fall in blood pressure. In 3 other patients the cold pressor test led to an abnormal reaction, but when the peridural anesthesia was administered the blood pressure values were absolutely normal. In these cases the patients were juveniles who had elastic vascular systems.

Two types of curves were obtained. The first showed a normal course of the blood pressure curve under both the cold pressor test and peridural anesthesia. In the second type the vascular reaction to the cold pressor test was abnormal. The blood pressure curve was unstable and did not return to the normal value. In 1 such case the condition of the blood pressure under peridural anesthesia showed the value of the test. After the fourth injection of pontocaine there was a fall in blood pressure. Veritol was given and the blood pressure value rose immediately to above 200 mm. Thereafter it slowly fell again to a low of 100 mm. Hg. At this time the patient showed the picture of circulatory collapse with involvement of the respiratory center. Veritol was given intravenously and raised the blood pressure so that the projected operation was feasible, even in this 42 year old patient.

There were no postoperative complications.

The results of this research show that with the cold pressor test one can ascertain the indications for peridural anesthesia. In the author's clinic, they operated upon women with carcinoma who were in generally poor condition, with anemia and hypo- and hypertension if the result of the cold pressor test was normal, using peridural anesthesia, and they observed no circulatory complications. If one has ever noted how rapidly a circulatory collapse can occur under peridural anesthesia and how under certain circumstances it is almost impossible to combat it, the search for a worthwhile prophylaxis is understandable. In the author's clinic the cold pressor test has been used since May, 1947 before each peridural anesthesia and it has been found to be a method with which they may predict unfavorable reactions to peridural anesthesia. If now peridural anesthesia be used only if the cold pressor test is normal, we may observe such overwhelming advantages that it may be used without many of the contraindications which previously have been prescribed.

(Anyone who has had experience with conduction anesthesia, whether it be caudal, spinal or lumbar peridural, has been frightened by the blood pressure drops which occasionally occur and would welcome some such screening process as the above, provided it is as dependable a guide as the author states. In the recent report by Andros, Dieckmann and their associates at the Chicago Lying-in Hospital on 719 cases of modified saddle block anesthesia, falls in systolic blood pressure between 40 and 49 mm. Hg. were noted in 4 per cent of cases and between 50 and 59 mm. Hg. in 1 per cent (*Am. J. Obst. & Gynec.* 55: 806, 1948). The systolic blood pressure fell below 80 mm. Hg. for a recordable period of time in 13.7 per cent of the patients receiving some anesthesia. Hingson has reported such a fall in 10 per cent of 2457 patients receiving continuous caudal anesthesia at the Philadelphia Lying-in Hospital.

These falls are rarely alarming in so far as the mother is concerned, but if protracted must inevitably exert a deleterious effect on the circulation in the intervillous spaces with resultant anoxia to the fetus. If only we had some method of screening the 4 or 5 per cent of patients who are especially likely to show such drops in pressure, it would augment greatly the safety of conduction anesthesia.—Ed.)

SULFADIAZINE AND PENICILLIN PROPHYLAXIS IN CESAREAN SECTION

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Am. J. Obst. & Gynec., 56: 422-439, (Sept.) 1948

This paper concerns a portion of a large study now in progress at the New York Lying-in Hospital in which an attempt will be made to determine the value of prophylactic sulfadiazine and penicillin in obstetrical cases when infection may be anticipated. Previous reviews have indicated that the incidence of infection as a complication to pregnancy and labor ranges between 2.7 and 9 per cent. Prolonged labor has been found to be one of the most common predisposing factors in the infections of labor, and cesarean section is often the method of choice for delivery in such cases.

With these points in mind, prophylactic antibiotics were given to all patients undergoing a cesarean operation in order to determine the effect on morbidity. If morbidity can be adequately controlled with these drugs, longer periods of trial labor can be more safely withstood by the patient.

Sulfadiazine was administered by the oral and intravenous routes, depending upon the needs of the particular case. One gram was given every 4 hours by the oral route and 4 gms. of sodium bicarbonate accompanied each dose. No incident of alkalosis occurred. When the intravenous route was employed 2.5 gm. of sodium sulfadiazine dissolved in 1/6 molar sodium lactate was given every 12 hours. Penicillin was administered intramuscularly in doses of 20,000 units every 3 hours. Patients delivered by cesarean section during the year 1935, a period entirely unaffected by antibiotics, have been compared with patients delivered by cesarean section during 1944, when sulfadiazine was extensively employed, and 1946, when both sulfadiazine and penicillin were employed prophylactically.

No prophylaxis was employed in the 70 cases encountered in 1935. In 1944, of 119 cases 25 received sulfadiazine alone and in 1946, of 136 cases, 93 received one or both of the antibiotics during some phase of labor. The gross maternal morbidity in 1935, 1944 and 1946 was 50, 30 and 34 per cent, respectively. Although the morbidity remained approximately the same in 1944 and 1946, the number of sections with 12 and 24 hours or more of labor was considerably increased in the latter year. The increased use of trial labor was apparent.

When the severity of the infection and total period of morbidity were considered, a striking reduction was noted in the latter years. The most evident reduction in morbidity occurred in urinary tract infections, and only one mild urinary tract infection was observed in 1946. A moderate decrease in the incidence of wound infections was seen. The duration and incidence of intrauterine infections was also markedly decreased in 1944 and 1946.

There was a very definite and progressive increase in the number of sections

performed after 24 hours of labor. In 1935, only 3 sections were performed after a labor of 24 hours, while 16 such cases were operated in 1946. In 1946, with prophylactic therapy, the low cervical technique was elected most frequently, replacing the earlier use of the extraperitoneal method. In 1935, one patient had a labor of 65 hours, had a low flap section and died on the eleventh postoperative day of peritonitis. In 1946, 8 cases had labors of more than 48 hours and no deaths were encountered and the longest postpartum febrile elevation was 4 days.

Of the sections performed in 1946, 69 cases received combined antibiotic therapy prophylactically. When these cases are compared with those of the same period who did not receive prophylactic therapy, no striking difference in overall morbidity is noted. However, in those cases receiving no prophylaxis, if labor were prolonged a marked increase in morbidity was apparent. Many of the patients in the latter group were uncomplicated cases, and this factor strongly suggests that little is gained by routine prophylaxis in the elective section.

The gross fetal mortality in the total clinic population for the years 1935, 1944 and 1946 was 3.34, 2.51 and 1.80 per cent, respectively. This reduction in fetal mortality was undoubtedly associated with the increased number of cesarean sections after prolonged labor. Only one fetal death occurred in 1946 after prolonged labor, and this death was not due to infection.

Other factors such as improved operative techniques, type of anesthesia, recognition of the influence of anemia, etc., have all played a role in improving the outlook for safe delivery by cesarean section. However, the use of antibiotics to control infection has broadened the safe employment of the newer and simpler techniques and has reduced the need for cesarean hysterectomy. Longer periods of trial labor were possible with the use of these drugs and a reduction of morbidity due to infections was found. 10 figures.

(This is a valuable and timely paper since it touches upon one of the moot questions of present-day obstetrics, namely, what type of cesarean section is best for the potentially infected case. Here we do not mean mismanaged and neglected patients who are already febrile, but the woman who has been in labor for 24 or 48 hours, possibly with membranes ruptured, but who is not febrile. Can transperitoneal low flap section be used without imposing additional risk because of the prolonged labor or is an extraperitoneal procedure or cesarean hysterectomy mandatory? The authors advance convincing evidence that the transperitoneal low flap section can be done safely in such cases provided adequate sulfadiazine and penicillin have been used prophylactically. This conforms with my own experience as stated in previous editorial notes.

From a bacteriological viewpoint one of the important points at issue here is whether the anaerobic streptococcus, the most important cause of puerperal infection, is vulnerable to penicillin. This question seems to have been answered in the affirmative by a study recently completed in our Department by Guilbeau, Schaub and Andrews. The uterine cultures were taken from 86 postpartum patients, 54 of whom received varying amounts of penicillin in labor and 32 of whom received no antibiotic therapy. From 30 of the 32 cultures in the control series from untreated patients, various bacteria were isolated, predominantly anaerobic streptococci and bacteroides. Of the uteri of 54 patients who had received penicillin therapy in labor, 32 were sterile aerobically and anaerobically, and 8 yielded only pleuropneumonia-like organisms,—bacteria which are generally regarded as non-pathogenic. Only 14 cultures in the penicillin series showed significant bacteria, 4 of which were penicillin-resistant coliform organisms. All but 1 of the penicillin-sensitive

organisms occurred in cultures taken more than 48 hours after delivery, from patients who had received small amounts of penicillin. This study not only shows that most strains of the anaerobic streptococcus are vulnerable to penicillin but indicates also that relatively high dosages of penicillin, given pre- and postpartum, may eliminate penicillin-sensitive organisms from the uterus for at least 3 days or more postpartum, and that a small amount (200,000 units) given early may be effective up to 48 hours following delivery.—Ed.)

THE HYDROSTATIC BAG IN OBSTETRICS

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Am. J. Obst. & Gynec., 56: 781-789, 1948

Because of the debatable place the use of the hydrostatic bag has in modern obstetrics, an analysis was made of the use of the bag over a ten-year period in which the same bag was used and the procedures did not vary.

A brief history of the bag and the disadvantages of the nonelastic bag are presented. The bag used in this series was a variation of the Braun bag molded from one piece of latex and pliable enough to vary its contour depending upon the pressure gradients upon it. This bag was only one size and could be introduced into a cervix where only 2 cms. of dilatation existed. The collapsed bag is folded and grasped with a curved sponge stick and introduced into the cervical os. The bag is attached to a Kelly bottle by rubber tubing and filled with sterile water to the desired size.

Of 22,935 deliveries, 244 were aided by the bag. The policy of this hospital, Cincinnati General Hospital, is conservative, which explains this incidence of one per cent. Indications for the use of the bag were bleeding, dilatation and toxemia.

Bleeding was the greatest indication for the use of the bag. In 64 cases of placenta previa, 12 were central placenta previa and 7 of the infants died. Therefore the use of the bag in cases of central placenta previa was discontinued. Placenta previa partialis, and occasionally marginalis, responds well to the use of the bag. The bag was used 23 times for abruptio placentae and only 3 of the infants lived, but the majority had no fetal heart beat on admission. The authors feel that this condition in multigravidas is a primary indication for the use of the bag since the infant has usually expired in utero and the cervix is often partially dilated. Seven cases of partial separation of the placenta were treated with the bag.

The second group included the patients in whom the bag was used to secure full cervical dilatation. The bag was chosen after the elimination of cephalopelvic disproportion as a factor. Fifty-four cases of uterine inertia or cervical dystocia were delivered. Breech, mostly the footling variety, and transverse presentations were other indications.

Since toxemia is best treated conservatively, medical induction and stripping of the membranes were tried before the bag was employed. In this group, 20 pre-eclamptics and 14 eclamptics were delivered with 18 living babies.

In this series there was a total of 253 infants. Spontaneous birth and podalic version were the predominant types of delivery.

Puerperal infection frequently follows the use of the bag. In this study 86 patients were classified as infected. Regular use of the antibiotics could have reduced the maternal morbidity. Prolapse of the cord resulted in 6 infant deaths and this might have been overcome by more careful auscultation of the fetal heart after the bag was in place.

The gross fetal mortality was 43%, and corrected by the exclusion of abnormalities incompatible with life and macerated nonviable fetuses, the percentage was 25. This included premature births. There were 87 premature infants and 52 of these were stillborn or died neonatally. There were 4 maternal deaths; however, no relationship between the use of the bag and the cause of death could be demonstrated.

The authors conclude that there is still a place for the use of the hydrostatic bag in obstetrics, but the selection of the correct bag and the type of patient is of paramount importance. 4 figures.

Maternal Mortality Reports

(Secretaries of Maternal Mortality Committees are invited to submit selected cases of maternal deaths, with analyses appended, for publication in this section of the Survey. Cases should be chosen on the basis of educational value, not because of rarity. For obvious reasons complete anonymity will be maintained.

Readers should note that the comment which follows each case history represents the opinion of the Committee concerned and does not necessarily reflect the attitude of the Editors.)

CASE NO. 72

The patient was a 25 year old white primigravida, whose EDC was February 27. She was first seen at the beginning of her eighth month of pregnancy, and made a total of four prenatal visits to her physician. Findings during her prenatal course were entirely normal with the exception of the fact that the patient was moderately undernourished and that her teeth showed considerable caries. The patient's membranes ruptured spontaneously at 8:P.M. on February 25, and she was admitted to the hospital two hours later, at which time general physical condition revealed the following:

Temperature, pulse and respirations normal; blood pressure 125/80; chest clear. The teeth showed moderate caries, and examination of the abdomen revealed a term-sized infant with the head dipping into the pelvis, and the fetal heart audible in the left upper quadrant at 144 per minute. The diagonal conjugate had previously been measured as 13 cm. and the pelvic outlet was said to be "wide." The patient was not in labor at the time of admission.

On the following morning at 9:00 A.M. the patient was having weak irregular pains approximately every 15 minutes. On rectal examination the cervix was well effaced with the external os 2 cm. dilated and the vertex presenting 3 cm. above the spines. The fetal heart was regular and of good quality. At noon on February 26 the pains were occurring every five minutes but were of short duration and ineffectual. The fetal heart remained good, but there was no further dilatation of the cervix on rectal examination. At 8:00 P.M. it was noted that the patient was draining greenish colored amniotic fluid. Pains were still irregular, averaging approximately every ten minutes. The fetal heart was still of good quality and regular.

At 8:00 A.M. on February 27, thirty-six hours after admission, pains were still weak and irregular. X-ray pelvimetry was obtained at this time revealing the obstetrical conjugate to be 10.5 cm. The patient's general condition was good. At 9:00 A.M. the fetal heart was counted at 80, and rectal examination revealed that there had been no further dilatation of the cervix or descent of the head. At 9:30 A.M. on February 27 the fetal heart could no longer be heard. Immediate classical cesarean section was performed, with the delivery of a living term male infant in good condition. No difficulties were encountered at the time of operation, the procedure requiring 45 minutes. During operation the patient was given 500 cc. of 5% glucose, and 100,000 units of penicillin. This was followed by 500 cc. of whole blood. Operation was performed under gas-oxygen-ether. Her condition immediately following operation was fair, but one hour later she had failed to respond and the pulse became thready, and there were signs of shock, the patient being cold, clammy, and cyanotic in spite of constant oxygen and stimulants. There was no vaginal bleeding. At 2:00 P.M. on the day of operation another 500 cc. of whole blood was given intravenously and she was kept in constant oxygen and given stimulants. Respirations ceased at 3:30 P.M. the day of operation without the patient having regained consciousness.

COMMENT

Although no temperature readings subsequent to admission to the hospital are listed in this patient's record, it would seem quite likely that intrapartum infection was present, particularly since it is mentioned that the amniotic fluid was colored. On reviewing this case history the committee felt this death should be classed as preventable on the following grounds; first and foremost the fact that the patient was not given, according to her record, any supportive therapy during the thirty-six hours of desultory labor. She was not rested, nor were intravenous fluids or penicillin given until it was obvious that the situation had become critical. Second, it was felt that the choice of type of section was in error and that the low cervical operation would have been far safer and less shocking to the patient. Third, in view of the frequent association of uterine inertia with cephalo-pelvic disproportion x-ray pelvimetry should have been carried out much earlier, in spite of the clinically normal diagonal conjugate measurement. Premature rupture of the membranes plus failure of the head to descend is enough to make one at least suspicious of disproportion, and earlier cesarean section would have carried with it infinitely less risk to both mother and child.

CASE NO. 73

The patient was a 26 year old colored para 0 who was first admitted to the hospital in April complaining of vaginal bleeding following a period of two months amenorrhea. The details of that admission are unknown except that the patient was treated conservatively as a case of incomplete abortion and was discharged several days after admission as improved. On June 15 she was re-admitted to the hospital complaining of nausea, vomiting, severe constipation, abdominal distention and pain. On her second admission examination revealed a markedly dehydrated, poorly nourished female with marked distention of the abdomen. Examination of the latter revealed a semi-solid mass filling the lower abdomen and rising to the level of the umbilicus and extending up into the left upper quadrant. The patient was given general supportive therapy and 7 days after admission exploratory laparotomy was carried out through a midline incision. At operation a large cystic mass was found in the lower abdomen filling the pelvis and extending well up into the left upper quadrant. This mass contained 1,000 cc. of clotted necrotic blood plus a 10 cm. macerated fetus. The mass was removed as completely as possible, together with the necrotic material including infected placental tissue. Two Penrose drains were inserted and the abdomen closed. While on the operating table the patient received 500 cc. of whole blood.

For the first week after operation her condition was satisfactory, but on the 8th postoperative day she began running a temperature of 102 to 103°. In spite of chemotherapy, frequent blood transfusions and plasma, intravenous fluids and other supportive therapy, the patient's condition gradually went downhill and respirations ceased on July 20, approximately 4 weeks after operation.

COMMENT

Diagnosis of extra-uterine pregnancy is admittedly often difficult and often not made with certainty until the time of laparotomy. In this case, however, the committee felt that there had been neglect in not having performed a careful pelvic examination on the patient prior to her release from the hospital on her original admission. Had such been done an extra-uterine mass would have been felt and the proper diagnosis made. In addition, no attempt at follow-up was

made on this patient, and even in those cases where one does not suspect ectopic pregnancy, patients under treatment for threatened or incomplete abortion should be followed long enough to insure their recovery. This was voted a preventable death on the basis of failure to make the proper diagnosis and to carry out a follow-up of the patient on her first admission.

CASE NO. 74

This patient was a 32 year old colored multipara with 9 previous pregnancies, 2 terminating in spontaneous abortions and the other 7 in living children. Her previous pregnancies had been entirely uncomplicated except for a history of pyelitis in one of the previous term pregnancies. The patient's EDC in her current pregnancy was October 24. She made her first prenatal visit during the second month and made a total of five such visits. All findings during the prenatal course were entirely normal including blood pressure, urinalysis, and weight. On the 14th of August the patient called her physician stating that she was having severe abdominal pain. She was seen shortly thereafter in her home, at which time the temperature, pulse, and respirations were normal, but examination revealed that the uterus was very tense. There was no external vaginal bleeding. A tentative diagnosis of premature separation of the placenta was made, and the patient was admitted to the hospital. Soon after admission the patient had several chills with temperature going to 104°. There was slight vaginal bleeding, the uterus remaining extremely tonic. The fetal heart could not be heard. The patient's pulse rate rose to approximately 100 per minute. She was started on penicillin 50,000 units every 3 hours, and within 24 hours her condition was much improved. The temperature returned to normal and remained there, vaginal bleeding ceased, and the uterus became soft on palpation. The fetal heart still could not be heard.

The patient remained in the hospital for another 72 hours, at the end of which time she insisted on leaving the hospital against advice. At the time of her discharge the temperature, pulse and respirations were normal, there was no vaginal bleeding and there were no symptoms. She returned home on August 19. On August 20 the patient was re-admitted having delivered en route to the hospital a stillborn fetus, and the placenta. She was given 1 cc. of an ergotrate preparation intramuscularly following her admission by the nurse on duty. A short time later it was noted by the nurse that there was profuse vaginal bleeding, and that the patient appeared restless and apprehensive. Before further treatment could be instituted she was pronounced dead 35 minutes after her arrival in the hospital. Permission for autopsy was not obtained.

COMMENT

Even though she was asymptomatic and apparently in satisfactory general condition, this patient should not have been allowed to leave the hospital undelivered with a probable diagnosis of premature separation of the placenta, though she apparently had escaped the critical clinical picture often associated with this condition. Although this patient is said to have left the hospital "against advice," the committee felt that this did not free the physician of all responsibility in the outcome. Usually, if pains are taken to describe the situation clearly, patients can be persuaded to follow their doctor's advice. This death occurred in a small rural hospital, and as is usually the case in such, there was no house staff. The patient was admitted by a nurse and was not seen by her physician until after her death, although the physician had been informed of her admission immediately and had been told her condition was satisfactory.

Knowing her probable diagnosis, the committee felt that the physician should have gone to examine her as soon as he was informed of her admission, since cases of premature separation are particularly prone to have postpartum hemorrhage. This was voted a preventable death.

CASE NO. 75

The patient was a 34 year old white para 4 with 4 living children whose previous obstetrical history was entirely negative. With her current pregnancy she made only two prenatal visits to her physician, the first one being during the 7th month. At the time of these visits all findings were normal. She fell into labor spontaneously approximately one week before her EDC, and was seen shortly thereafter in her home by her attending physician, and labor was found to be progressing satisfactorily at that time. At 5:15 A.M. on November 7, after the patient had been in labor for approximately 4 hours she was given 2 cc. of pituitrin intramuscularly. Shortly thereafter the patient suddenly turned deeply cyanotic and respirations ceased. At the time of this accident no drugs other than the pituitrin had been given and the patient was not receiving anesthesia. In spite of continuous oxygen and adrenalin, the patient was pronounced dead at 6:00 A.M. on November 7. Permission for autopsy was not obtained. The cause of death as given on the death certificate was listed as acute embolism. The patient died undelivered 45 minutes after the administration of pituitrin.

COMMENT

It is impossible to obtain reliable statistics on the use of pituitrin in labor in the hands of physicians throughout the country. There are no doubt many cases such as this in which the fact that pituitrin was given is never known and the death is charged to one or another of a variety of causes such as embolism. It was felt in reviewing this case that there was no indication for the administration of pituitrin, that the dose given was 15 times the maximum safe initial dose if pituitrin is to be used, and that there was a distinct possibility* that death was due either to rupture of the uterus or to acute coronary spasm caused by sensitivity to pituitrin. On the above grounds the death was voted preventable.

CASE NO. 76

This patient was a 31 year old white para 2 with 2 living children, whose EDC with the current pregnancy was August 15. She had received regular prenatal care since the beginning of the 5th month of pregnancy, and had made a total of eight prenatal visits, at which time all findings were entirely normal. On July 2 the patient's membranes ruptured spontaneously and prematurely. It is not known whether the patient consulted her physician concerning this or not, but 8 days later, on July 10, she was admitted to the hospital because of a temperature elevation to 101°. On admission the patient's general condition was otherwise satisfactory and an estimated 4 lb. infant of 34 weeks duration lay in vertex presentation with the fetal heart audible. She was immediately begun on penicillin 100,000 units every 3 hours. On the day following admission she fell into labor spontaneously, and after a precipitate labor delivered spontaneously a premature infant weighing 4½ pounds. The patient was delivered by the attending nurse and was seen 10 minutes after delivery by her physician. At that time the placenta had separated and was easily expressed and 1 cc. of ergotrate was given intramuscularly, but she continued to bleed rather freely. Accordingly, she received a second cc. of ergotrate intravenously 15 minutes later. Following the intravenous ergotrate the uterus contracted well and bleeding became minimal. Up to this time the total blood loss was estimated at 500 cc. Her physician remained in the

made on this patient, and even in those cases where one does not suspect ectopic pregnancy, patients under treatment for threatened or incomplete abortion should be followed long enough to insure their recovery. This was voted a preventable death on the basis of failure to make the proper diagnosis and to carry out a follow-up of the patient on her first admission.

CASE NO. 74

This patient was a 32 year old colored multipara with 9 previous pregnancies, 2 terminating in spontaneous abortions and the other 7 in living children. Her previous pregnancies had been entirely uncomplicated except for a history of pyelitis in one of the previous term pregnancies. The patient's EDC in her current pregnancy was October 24. She made her first prenatal visit during the second month and made a total of five such visits. All findings during the prenatal course were entirely normal including blood pressure, urinalysis, and weight. On the 14th of August the patient called her physician stating that she was having severe abdominal pain. She was seen shortly thereafter in her home, at which time the temperature, pulse, and respirations were normal, but examination revealed that the uterus was very tense. There was no external vaginal bleeding. A tentative diagnosis of premature separation of the placenta was made, and the patient was admitted to the hospital. Soon after admission the patient had several chills with temperature going to 104°. There was slight vaginal bleeding, the uterus remaining extremely tonic. The fetal heart could not be heard. The patient's pulse rate rose to approximately 100 per minute. She was started on penicillin 50,000 units every 3 hours, and within 24 hours her condition was much improved. The temperature returned to normal and remained there, vaginal bleeding ceased, and the uterus became soft on palpation. The fetal heart still could not be heard.

The patient remained in the hospital for another 72 hours, at the end of which time she insisted on leaving the hospital against advice. At the time of her discharge the temperature, pulse and respirations were normal, there was no vaginal bleeding and there were no symptoms. She returned home on August 19. On August 20 the patient was re-admitted having delivered en route to the hospital a stillborn fetus, and the placenta. She was given 1 cc. of an ergotrate preparation intramuscularly following her admission by the nurse on duty. A short time later it was noted by the nurse that there was profuse vaginal bleeding, and that the patient appeared restless and apprehensive. Before further treatment could be instituted she was pronounced dead 35 minutes after her arrival in the hospital. Permission for autopsy was not obtained.

COMMENT

Even though she was asymptomatic and apparently in satisfactory general condition, this patient should not have been allowed to leave the hospital undelivered with a probable diagnosis of premature separation of the placenta, though she apparently had escaped the critical clinical picture often associated with this condition. Although this patient is said to have left the hospital "against advice," the committee felt that this did not free the physician of all responsibility in the outcome. Usually, if pains are taken to describe the situation clearly, patients can be persuaded to follow their doctor's advice. This death occurred in a small rural hospital, and as is usually the case in such, there was no house staff. The patient was admitted by a nurse and was not seen by her physician until after her death, although the physician had been informed of her admission immediately and had been told her condition was satisfactory.

Knowing her probable diagnosis, the committee felt that the physician should have gone to examine her as soon as he was informed of her admission, since cases of premature separation are particularly prone to have postpartum hemorrhage. This was voted a preventable death.

CASE NO. 75

The patient was a 34 year old white para 4 with 4 living children whose previous obstetrical history was entirely negative. With her current pregnancy she made only two prenatal visits to her physician, the first one being during the 7th month. At the time of these visits all findings were normal. She fell into labor spontaneously approximately one week before her EDC, and was seen shortly thereafter in her home by her attending physician, and labor was found to be progressing satisfactorily at that time. At 5:15 A.M. on November 7, after the patient had been in labor for approximately 4 hours she was given 2 cc. of pituitrin intramuscularly. Shortly thereafter the patient suddenly turned deeply cyanotic and respirations ceased. At the time of this accident no drugs other than the pituitrin had been given and the patient was not receiving anesthesia. In spite of continuous oxygen and adrenalin, the patient was pronounced dead at 6:00 A.M. on November 7. Permission for autopsy was not obtained. The cause of death as given on the death certificate was listed as acute embolism. The patient died undelivered 45 minutes after the administration of pituitrin.

COMMENT

It is impossible to obtain reliable statistics on the use of pituitrin in labor in the hands of physicians throughout the country. There are no doubt many cases such as this in which the fact that pituitrin was given is never known and the death is charged to one or another of a variety of causes such as embolism. It was felt in reviewing this case that there was no indication for the administration of pituitrin, that the dose given was 15 times the maximum safe initial dose if pituitrin is to be used, and that there was a distinct possibility that death was due either to rupture of the uterus or to acute coronary spasm caused by sensitivity to pituitrin. On the above grounds the death was voted preventable.

CASE NO. 76

This patient was a 31 year old white para 2 with 2 living children, whose EDC with the current pregnancy was August 15. She had received regular prenatal care since the beginning of the 5th month of pregnancy, and had made a total of eight prenatal visits, at which time all findings were entirely normal. On July 2 the patient's membranes ruptured spontaneously and prematurely. It is not known whether the patient consulted her physician concerning this or not, but 8 days later, on July 10, she was admitted to the hospital because of a temperature elevation to 101°. On admission the patient's general condition was otherwise satisfactory and an estimated 4 lb. infant of 34 weeks duration lay in vertex presentation with the fetal heart audible. She was immediately begun on penicillin 100,000 units every 3 hours. On the day following admission she fell into labor spontaneously, and after a precipitate labor delivered spontaneously a premature infant weighing 4½ pounds. The patient was delivered by the attending nurse and was seen 10 minutes after delivery by her physician. At that time the placenta had separated and was easily expressed and 1 cc. of ergotrate was given intramuscularly, but she continued to bleed rather freely. Accordingly, she received a second cc. of ergotrate intravenously 15 minutes later. Following the intravenous ergotrate the uterus contracted well and bleeding became minimal. Up to this time the total blood loss was estimated at 500 cc. Her physician remained in the

hospital for another half hour and checked the patient prior to leaving and found the uterus firm and the patient's condition outwardly satisfactory. A nurse was left in charge of the patient and the physician returned to his office. He received a call thirty minutes after leaving the hospital informing him that the patient had had a sudden massive vaginal hemorrhage, and on reaching the hospital found that the patient had expired.

COMMENT

For many years the teachers of obstetrics have been stressing that; 1) the first hour or two following delivery constitute a critical time for every mother, 2) blood loss is difficult if not impossible to *estimate*, and 3) modern obstetrics demands adequate facilities for prompt blood transfusion. In reviewing this case the committee felt that the attending physician neglected to check the condition of his patient with care—there is no record of pulse rate or blood pressure—, that he did not remain with his patient long enough to be certain her condition was satisfactory, and that no effort was made to replace the blood loss, or prepare for blood transfusion in the event of further excessive hemorrhage. In the state in which this death occurred, hemorrhage has become the major cause of maternal mortality, accounting for approximately 50% of maternal deaths. Careful observation and treatment of patients who bleed, *anticipation* of the need for blood transfusion, and blood banks will prevent unnecessary deaths such as this.

CASE NO. 77

The patient was a 17 year old colored primigravida due by dates on November 24. She first consulted her physician on August 15, at which time physical examination was entirely negative except for an enlarged uterus corresponding to an approximate 26 weeks pregnancy. The blood pressure was 110/70 and urinalysis was negative. The patient, however, weighed 152 pounds and stated that her normal non-pregnant weight was 118 pounds. Apparently no dietary instruction was given, nor was the patient warned about the excessive weight gain. Following this original examination she failed to make any further prenatal visits to the physician of her choice, and was not seen again until November 20, when she complained of intermittent uterine contractions occurring every three minutes. She was admitted at 5:30 A.M. on that date to her physician's three-bed hospital which he maintains for the care of maternity patients. On admission temperature was 98.6°, respirations 33, blood pressure 150/80, with uterine contractions occurring every three minutes. Catheterized urine specimen revealed a 2 plus albuminuria. The patient was given 42 grains of nembutal by mouth immediately after admission. At 7:00 A.M. the blood pressure was 160/82. At this time she received intravenous magnesium sulphate, dosage not stated. At 10:30 A.M. the patient had a generalized convulsion, the blood pressure being 190/120 at that time. She then received morphine sulphate grains $\frac{1}{2}$ and 50 cc. of 50% glucose intravenously. Six grains of nembutal were administered rectally. At 11:00 A.M. the blood pressure was 150/72, and the patient received 1,000 cc. of 10% glucose in water intravenously. At 12:30 P.M. the blood pressure was 170/100, and another 4½ grains of nembutal were administered rectally. The patient was having uterine contractions every five minutes.

At 1:00 P.M. the patient had a second convulsion and was given another $\frac{1}{2}$ grain of morphine sulphate and more magnesium sulphate intravenously. The temperature at this time was 100.2, pulse 80, respirations 40, and blood pressure 160/82. At 3:15 P.M. she was delivered spontaneously of a normal living female infant weighing 7½ pounds. Following delivery of this child a second infant was discovered presenting by breech. More magnesium sulphate was given intravenously, and at 6:15 P.M., three hours after delivery of the

first child the second infant was delivered by breech extraction, and although in poor condition, was resuscitated.

The mother's condition following delivery of the second child was as follows: blood pressure 100/72, pulse 60, respirations 18, with the patient appearing very drowsy. At 6:45 P.M. the patient was in deep coma. She was given more magnesium sulphate intravenously and another 1,000 cc. glucose in water. Respirations ceased at 7:10 P.M., 55 minutes after delivery of the second child.

COMMENT

Deaths from eclampsia are fortunately becoming less and less frequent. In this particular case the patient's weight gain of 34 pounds by the 26th week of pregnancy was apparently overlooked. Following that initial error, the patient received no further prenatal care. This fact, however, can be blamed largely on the patient herself, but the committee in reviewing this case felt that the physician was equally culpable, and that he should have made strenuous efforts to persuade the patient to return for regular prenatal visits.

In reviewing the therapy given this patient after her admission in labor, it was felt definitely that the patient received too much sedation. The dosage of magnesium sulphate is not given, but any appreciable quantity of this drug plus the large amounts of morphine and nembutal administered was excessive. Further supportive therapy such as digitalis and constant oxygen should have been given. This death was accordingly classified as preventable.

Gynecology

ENDOCRINOLOGY

INACTIVATION OF OESTROGENIC HORMONE BY WOMEN WITH VITAMIN B DEFICIENCY

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J. Obst. & Gynaec. Brit. Emp., 55: 273-280 (June) 1948

It has been demonstrated both *in vivo* and *in vitro* that the liver, and to a lesser extent, the spleen and perhaps the kidneys are the only organs in the body which can inactivate the estrogenic hormone. It has been claimed that estrogen inactivation is dependent on the adequate intake of vitamin B complex. It has been assumed that a deficiency of vitamin B complex deprives the liver of its ability to inactivate estrogenic substances. Certain hyperestrogenic disturbances have thus been attributed to vitamin B complex deficiencies and claims have been made that they responded to therapy with this vitamin.

During the war years the authors had an opportunity to observe a great many women, both pregnant and non-pregnant, with vitamin B deficiencies, and they selected 14 of these cases for intensive study of the relationship of the deficiency to estrogen metabolism. These women were divided into 3 groups: (1) those menstruating regularly with evidence of vitamin B deficiency; (2) those in whom symptoms of deficiency occurred during pregnancy; and (3) those whose symptoms appeared during pregnancy and were further complicated by a severe hepatitis.

In the first group there was no clinical evidence of abnormal genital function and menstruation was normal in all respects. No cases of hyperestronemia manifested by enlarged uterus, cystic follicles or cystic mastitis were observed. In all cases, endometrial biopsy showed the normal histological pattern and vaginal smears showed no evidence of increased estrogen activity. The estrogen levels of blood and urine were normal and the estrone clearance test showed that the inactivation of estrone was similar to that found in women without signs of vitamin B deficiency.

The clinical histories of the 6 pregnant women in the second group revealed that in 2 of these cases deficiency syndromes had been present for at least one year. Estrogen levels in blood and urine were no higher than in corresponding months of normal pregnancy. The estrone clearance test showed normal inactivation of injected estrone.

In 2 cases of pregnancy, vitamin B deficiency was associated with severe liver damage due to infectious hepatitis, the deficiency syndrome having appeared dur-

ing the course of the disease. The blood and urine estrone levels were normal. Furthermore, additional estrone administered was rapidly inactivated in the body as shown by the estrone clearance test.

The authors conclude that inactivation of endogenous and exogenous estrogen remains unimpaired in vitamin B deficiencies in pregnant and non-pregnant women. Since no changes in estrogen inactivation were observed in women suffering from severe vitamin B deficiencies, the vitamin seems not to be an essential factor in the estrogen inactivating mechanism.

(During the past two years or so much has been written about the supposed role of vitamin B deficiency in interfering with the estrogen inactivating role of the liver, based chiefly on the work of the Biskinds. This liver incapacity has therefore been stressed as a cause of hyperestrogenism, and on this theory various disorders, such as functional uterine bleeding, have been treated with vitamin B. Now we have two well qualified investigators, one of them identified with important advances in endocrinology, coming along to tell us that vitamin B deficiency in either the non-pregnant or the pregnant woman has no effect at all upon the estrogen-inactivating function of the liver, and the clinical experiments upon which they base this conclusion seem sound and well-conceived. As with so many other questions bearing upon the management of functional disorders, we poor clinicians wish that the laboratory investigators would make up their minds, though we are equally divided among ourselves as to the management of many clinical problems of non-endocrine nature.—Ed.)

THE USE AND MISUSE OF HORMONES IN OBSTETRICS AND GYNECOLOGY

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J. M. Soc. New Jersey, 45: 278-282 (June) 1948

Properly employed, the sex hormones are valuable weapons in our armamentarium. Improperly and indiscriminately used, they will produce unfavorable reactions and may harm the patient and the reputation of the doctor. It is only by vigorously opposing the injudicious use of hormones that their valuable assets may be preserved.

Proper endocrine therapy necessitates a correct diagnosis. This cannot be determined by clinical observation alone. Many stigmata formerly believed to be indicative of specific endocrinopathies are now recognized to be of constitutional origin.

Having made an etiologic diagnosis, the physician must determine whether hormonal therapy is the rational method of approach, even if he can demonstrate a pituitary or ovarian disturbance. The pituitary-ovarian cycle is a very labile one, influenced early in the onset of many organic diseases, dysfunctions, and metabolic disturbances and sensitive to neurogenic and psychogenic factors of all sorts.

Gynecology

ENDOCRINOLOGY

INACTIVATION OF OESTROGENIC HORMONE BY WOMEN WITH VITAMIN B DEFICIENCY

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Laboratory of the Hebrew University, Jerusalem, Palestine*

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It has been demonstrated both *in vivo* and *in vitro* that the liver, and to a lesser extent, the spleen and perhaps the kidneys are the only organs in the body which can inactivate the estrogenic hormone. It has been claimed that estrogen inactivation is dependent on the adequate intake of vitamin B complex. It has been assumed that a deficiency of vitamin B complex deprives the liver of its ability to inactivate estrogenic substances. Certain hyperestrogenic disturbances have thus been attributed to vitamin B complex deficiencies and claims have been made that they responded to therapy with this vitamin.

During the war years the authors had an opportunity to observe a great many women, both pregnant and non-pregnant, with vitamin B deficiencies, and they selected 14 of these cases for intensive study of the relationship of the deficiency to estrogen metabolism. These women were divided into 3 groups: (1) those menstruating regularly with evidence of vitamin B deficiency; (2) those in whom symptoms of deficiency occurred during pregnancy; and (3) those whose symptoms appeared during pregnancy and were further complicated by a severe hepatitis.

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HYPERESTROGENISM TREATED WITH LACTOGENIC HORMONE (PROLACTIN)

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J. Clin. Endocrinol., 8: 613 (July) 1948

In this paper the hyperestrogenic syndrome is considered an actual clinical entity. Diagnosis of the condition may be accomplished either by clinical examination or by laboratory tests (smear or biopsy).

Thirty-nine cases were studied; all strictly corresponded to the picture of hyperestrogenism and were checked by means of the vaginal smear.

These patients were treated with lactogenic hormone, the action of which is anti-estrogenic, luteotropic and regulatory of hormonal balance. The patients were injected for monthly series, for one to 7 series. The total dosage ranged from 720 units given in 12 days, to 2700 units given in 15, 18 or 21 days.

Good results were obtained in 25 cases (64%); fair in 7 (18%); and there was no improvement in 7 (18%). From these 39 cases, 69 different syndromes were studied, some patients showing more than one. Nervous and mental symptoms and premenstrual tension reacted very well to lactogenic hormone. Migraine and leucorrhea, particularly the former, disappeared. Most patients improved.

Consequently, the lactogenic hormone of the pituitary gland is an effective means to control hyperestrogenism, whatever its clinical picture.

(If the author's concept of hyperestrogenism includes such varied clinical conditions as nervous and mental symptoms, premenstrual tension, migraine and leucorrhea, one wonders as to the rationale of the clinical examination and the laboratory tests which he says make such a diagnosis possible. If, for example, a woman with leucorrhea happens to have a so-called hyperestrogenism on the basis of hormone studies of the urine, or vaginal smears, or endometrial biopsies, all of which methods have been found to be of very limited value in most other clinical fields, is it to be assumed that the leucorrhea is of hyperestrogenic etiology? One might as reasonably say that a woman whose bowels move after a dose of cascara was suffering with hypocalcemia. Moreover, it is quite certain that anti-estrogenic therapy would be less effective for the leucorrhea than cascara for the constipation.)

Hyperestrogenism may produce just as opposite clinical symptoms as amenorrhea and hypermenorrhea, and functional gynecological disturbances are not usually to be explained on a simple plus or minus basis as far as estrogen is concerned. Moreover, the effectiveness of prolactin even in cases of undoubted hyperestrogenism needs far more proof than the author's small series of cases, comprising many different types. The exact role of prolactin in the physiology of lactation is still not altogether clear. The work of Meites and Turner appears to have cast serious doubt upon the earlier investigations of Nelson, which led to the theory that estrogen is the inhibitor of prolactin during pregnancy, and that it is only when this inhibition is removed by parturition that prolactin produces its lactating effect. Now it seems that estrogens are actually stimulants of the lactogenic hormone. The nature of the latter is still in doubt, especially as to its relation to luteotrophin, and some look upon them as identical.

In view of such considerations, I am frank to say that my own reaction to Villaverde's concept of hyperestrogenism as well, as the results of prolactin therapy for such a variety of clinical manifestations, is one of great skepticism.—Ed.)

Choice of a sex-hormone should be made on a rational plan of approach. For instance, a follicle-stimulating hormone may be rationally indicated in anovulatory sterility where there is reason to believe that the pituitary production of gonadotrophin is inadequate. On the other hand, gonadotrophic stimulation would be irrational in a similar patient who had all the evidences of a primary ovarian deficiency.

It must be admitted, however, that there are times when what may seem "irrational" therapy will accomplish the desired result. Thus, substitutional therapy with estrogens and progesterone may sometimes induce ovulation in a sterility patient if given in the proper dosage and in cyclic fashion. Many failures of endocrine therapy of functional menstrual disorders and sterility are the result of giving the proper hormones in inadequate dosage or at the improper time of the cycle.

Not all patients for whom certain hormones are rationally indicated are fit subjects for their administration. This point can be evaluated only by a familiarity with the untoward effects and over-dosage manifestations, as well as a knowledge of any conditions which may contraindicate their use.

The author summarizes the main indications and difficulties which may arise when hormones are improperly employed, in regard to various sex-hormones.

(The author very properly emphasizes that many body abnormalities parade as endocrinopathies which actually are of constitutional or genotypic nature. Any number of illustrations might be adduced. For example, a good many women are greatly distressed by abnormalities of hair growth, most often of the forearms and legs, frequently of the abdomen, and, most distressing of all, on the face. In a small minority such hirsutism is actually of endocrine causation, as in the rather rare cases of arrhenoblastoma or certain cortical tumors. In such cases the hair anomaly appears fairly abruptly in women who were previously quite normal, and it is accompanied by other endocrine manifestations of masculinizing type. Much more frequently the history reveals that the hirsutism made its appearance at about the time of puberty, and no other stigmata are present. Endocrine therapy in such cases is quite sure to be a waste of the patient's time and money. Abnormalities of height, including moderate gigantism, are often constitutional and even familial type. I recently saw a young woman of Amazonian build and nearly 6 feet tall. Inquiry revealed that her father and several brothers were giants of the same so-called Viking type—incidentally, this family was actually of Norwegian extraction.)

The author offers a modest justification for the empirical and substitutional organotherapy which I suppose every endocrinologist at times uses, although he should try to keep the brakes on in this respect. Everyone uses thyroid in certain cases of sterility, often on no established scientific basis, but frequently with good results. We have learned an enormous amount about reproductive physiology and about endocrinology, but organotherapy lags far behind the scientific bandwagon. While shotgun and random endocrine therapy can never be justified, one must not be too harsh with the endocrinologist who does the best he can with the still meager endocrine equipment at his disposal. As used to be posted on the wall of the old Western bar-rooms, "Don't shoot the piano player; he's doing the best he can."—Ed.)

THE SIMILARITY OF ESTROGENIC EFFECT IN PREMENSTRUAL TENSION, MENSTRUAL ANOMALIES, CHRONIC CYSTIC MASTITIS AND CANCER OF THE BREAST

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J. Clin. Endocrinol., 8: 613 (July) 1948

The author's previous studies have indicated that an estrogen-progesterone imbalance with a relative excess of estrogen is the major etiological factor in premenstrual tension, menstrual anomalies and chronic cystic mastitis. These clinical manifestations of increased cellular proliferation and retention of intracellular fluid have been duplicated by administering estrogen to castrates and normal women past the menopause. There has also been increasing evidence in the recent literature that continued estrogen secretion accelerates epithelial neoplasia and conversely, that diminution of high endogenous estrogenic activity by castration or the administration of large doses of testosterone, slows the progress of the cancerous growth.

In the current study the effect of estrogen is being investigated in patients with premenstrual tension, menometrorrhagia, chronic cystic mastitis and carcinoma of the breast. The stimulating effect of uninhibited estrogen on epithelial proliferation is demonstrated in the breast by the presence of intracystic papillomas and cyst formation and in the uterus by a highly proliferative or mixed endometrium which is characterized clinically by shortened menstrual cycles and increased bleeding. Evidence of cyst formation in the ovary is present in some cases. Increased interstitial fluid retention is manifested by painful distention of the breast, nausea and vomiting, dysmenorrhea, abdominal distention, headaches, syncope, irritability, and occasionally localized edema.

The clinical picture is correlated with breast and endometrial biopsies and vaginal smears. The urinary excretion of estrogen, pregnanediol and gonadotrophin is assayed. Determinations of calcium, potassium, sodium and sugar tolerance are made; and daily body weights and basal temperatures are recorded. Determinations of capillary permeability during and after the state of fluid retention are done by the florescein method.

An evaluation of the above findings and a discussion of certain implications is presented in this preliminary report.

(Although the effect of estrogens in the production of certain menstrual abnormalities and certain proliferative conditions in both the breast (chronic cystic mastitis) and endometrium (hyperplasia) has been pretty well established, the present study represents a comprehensive and well conceived plan of investigations on human beings rather than on the laboratory animals which have yielded much of our information on these various points. Especially interesting are the studies reported on premenstrual tension, apparently confirming the work of Thorne and others, which showed that, both in this and in premenstrual edema, retention of fluids is characteristically associated with the relative estrogen excess found in these conditions.—Ed.)

ABSORPTION AND EXCRETION OF CHORIONIC GONADOTROPHIN
WHEN ADMINISTERED INTRAMUSCULARLY TO WOMEN. A
COMPARISON OF AQUEOUS, OIL EMULSION AND OIL AND WAX
PREPARATIONS.

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J. Clin. Endocrinol., 8: 599 (July) 1948

This study investigated the relative rate of absorption of chorionic gonadotrophin from various injection media. A single dose of 10,000 I.U. was given intramuscularly to normal women and the rate of excretion in the urine was determined at 12-hour intervals up to 120 hours. The aqueous solution, Antuitrin-S, was made into an oil emulsion with Emulgen. The wax and oil preparation was A.P.L.

The urinary assays were made by injecting the test rats with urine in volumes equivalent to 1, 3, or 6 minutes' output. Positive assays were those in which definite corpora lutea were present at 96 hours.

Absorption from the aqueous solution was very rapid since urine volumes to a 3-minute output contained at least one rat unit by 12 hours. This rate was not reached until 12 to 24 hours after administering an oil emulsion or one in oil and wax. From 12 to 48 hours after administering the aqueous solution the excretion rate was such that a one minute output occasionally contained one rat unit. The oily media did not reach this value. From 48 to 72 hours the excretion rate was rather uniform irrespective of the media used. From 72 to 120 hours the excretion rate was greater when an aqueous solution was used.

These observations would suggest that the absorption from oily media may be too slow to result in optimum blood levels. It may be that the rate of elimination of this protein hormone through the human kidney is so slow that there is no real advantage in trying to delay its absorption at the site of injection.

(The authors of this paper have published a number of interesting reports on the therapeutic use of chorionic gonadotrophic substances, though I have the impression that the pregnancy hormone preparations are not occupying a very conspicuous role in the therapeutic field, not as important as many at one time hoped. It is of interest that the present study, unlike some of those made with estrogens, leads the authors to suspect that the slow absorption of the chorionic gonadotrophes may be a disadvantage rather than an advantage.—Ed.)

ically scirrhous carcinoma, but as no biopsy was performed, histologic confirmation was lacking.

Of the remaining 11 patients, 3 had relief from pain out of the 5 in which this was a marked symptom. The primary growth regressed in 2 patients and became static in one, while one showed regression of axillary metastases. However, only in 2 cases did the response exceed a 2 months' duration.

The treatment was given orally and toxic reactions were not severe. A possible interplay between the roles of surgery and hormone therapy in the treatment of the elderly patient is suggested.

(The average clinician is likely to be confused by some of the newer trends in the endocrine therapy of advanced breast cancer. On the one hand he is warned not to give estrogens to women who have so-called precancerous lesions of the breast, and he is advised to abolish estrogen function by castration or X-ray in cases of breast cancer during reproductive life. And now he is told to give large amounts of the estrogen diethylstilbestrol in advanced cancer, especially when there are bony metastases. This plan was obviously suggested by the good results of the same therapy in men with prostatic cancer and bone metastasis, not curative but often strikingly palliative. I do not believe that Huggins, who first suggested this valuable palliative therapy, has formed any satisfactory conclusions as to how the retarding effect is brought about, nor is any satisfactory explanation available for the possible palliative benefits of estrogen therapy in late mammary cancer. Large doses of estrogen do have an inhibitory effect upon the pituitary, but just how this could be helpful in cancer is not clear.

Even theoretically, it might be thought that the male sex hormone would be more logically used in these advanced cancers of the female breast, and, as a matter of fact, testosterone has been much more frequently employed for this purpose than has stilbestrol. The total reported number of cases thus treated is not as yet very large, the largest series being that reported by Adair from the Memorial Hospital in New York. The results in this series were considered sufficiently encouraging to warrant a continuance of the plan. It must be remembered that the dosage required is very large and expensive,—several hundred milligrams weekly. Disagreeable virilization symptoms are always to be expected, but this side effect of the treatment is considered to be a small price for the patient to pay for the relief from pain and the retardation of the disease which is often obtained.—Ed.)

THE USE OF THE VAGINAL SMEAR IN THE ASSAY OF ESTROGENS GIVEN ORALLY OR INTRAMUSCULARLY

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J. Clin. Endocrinol., 8: 612 (July) 1948

The laboratory method of estrogen assay in the castrate rat has been adapted to the woman past menopause in an effort to gain objective evidence of relative potencies of various estrogens in women. Groups of 10 to 20 women have been used at each dose level and the dose increased until the minimal effective dose was found. Vaginal smears were obtained once a week. The oil solutions were

MECHANISM OF INACTIVATION OF α -ESTRADIOL BY RAT LIVER "IN VITRO"

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J. Clin. Endocrinol., 8: 601 (July) 1948

The inactivation of estradiol was studied by incubating either rat liver slices (100 mg.) or homogenate (10 per cent) in 5 ml. of Krebs solution, phosphate buffer pH 7.4, without glucose for 2 hours at 37.5 C. Usually 1 γ of α -estradiol was used. The amount of biologically active material present at the end was determined by bioassay in mice.

Complete inactivation by liver slices was observed whether the gas phase was oxygen or air. In nitrogen or with boiled slices no inactivation took place.

The 10% homogenate prepared with the Waring blender or by crushing frozen liver to a fine powder produced from 40 to 70% inactivation. No change was observed when the Fuhrman and Crismon "intercellular medium" was substituted for the Krebs solution or when boiled liver extract or glucose was added to the medium.

The inactivation by liver slices was inhibited by capryl alcohol, but not by cyanide, azide, thiourea, malonate, fluoride, or monoiodoacetate. The addition of methylene blue to slices incubated in nitrogen brought about a 40 to 70% inactivation. Nicotinamide and DPN added to the homogenate increased the inactivation by 50%.

These results indicated that no appreciable inactivation is due to conjugation of the estradiol.

As a consequence of their findings, the authors conclude that the system cytochrome-cytochrome oxidase does not participate, or at least only to a very minor extent; and that the inactivation is probably produced by a dehydrogenating system or systems.

STILBOESTROL IN LATE MALIGNANT DISEASE OF THE BREAST

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Glasgow Med. J., 29: 248-254 (July) 1948

A discussion of the literature describing the use of stilbestrol in late inoperable carcinoma of the breast is given. Twelve such cases treated with stilbestrol are reported here.

Good results were obtained in 2 patients, both over 70 years and with a single ulcerating growth. There was one apparent cure of an ulcerating growth, clin-

tered to rats 21 to 25 days old, there is normal follicular development followed by ovulation and luteinization. Doses of 8 to 12 I.U. produce superovulation and superfecundity. When the same hormone is injected into 18-day-old rats a pure follicular response is obtained. When gonadotrophin is given to 10-day-old rats the response is limited to the interstitial tissue but there is enough estrogen produced to cause growth of the uterus and vagina.

These experiments demonstrate the difficulties that are encountered in using these hormones clinically where the physiological age of the patient is often obscure. Endometrial biopsies, vaginal smears and hormonal assays may increase the usefulness of these hormones. At present, there seem to be no widely accepted specific indications, but gonadotrophins have been used with varying success in hypogonadism in girls and young women. Failures have probably been encountered in prolonged treatment with gonadotrophins because of antihormone formation. This seems to be true only when the equine or crude preparations are used. The author feels that perhaps there are other gonadotrophic substances which as yet have not been discovered and that these new hormones might answer the problem of the refractory ovary.

(The author is not alone in suggesting that the large number of hormones ascribed to the anterior pituitary are really not separate principles, but that there is only a small group of cardinal principles which under different conditions and in various derivative forms produce the different hormonal effects attributed to separate substances. Riddle, for example, has long been a champion of this point of view. Cole's comments are limited to the gonadotrophic principles. While the duality of the two pituitary gonadotrophic principles, FSH and L, has been widely accepted, there are still some dissenters from this viewpoint. As to the chorionic gonadotrophin, the fact that it is produced in the trophoblast and not the pituitary makes it seem more difficult to believe that it is in any way derived from the 2 sex principles of the hypophysis.—Ed.)

given as a single intramuscular injection and the oral preparations were given daily for 10 days.

Stilbestrol given orally stimulated the vaginal mucosa in doses of 2.5 and 1.0 mg. per day, whereas 0.5 mg. per day gave only a minimal response. Stilbestrol given intramuscularly gave maximal responses in doses of 0.5 to 2.0 mg.

Estrone given orally produced maximal cornification changes at doses of 1 and 2 mg. per day; a dose of 0.5 mg. produced a minimal response.

Natural estrogens given orally produced a vaginal response at dose levels of 20,000 I.U. and 10,000 I.U. per day which were equivalent to the daily doses of stilbestrol. Natural estrogens were given intramuscularly in oil solutions and in aqueous solutions, and the response to 20,000 I.U. was comparable to that obtained with 1.0 mg. of stilbestrol. No difference could be noticed between the response to oil solutions and aqueous suspensions of large or small crystals.

Trimethyl Estradiol Acetate was the most potent estrogen tested, doses as low as 0.16 mg. giving a definite response.

(A great many studies of this general sort have been made to investigate the comparative value of various estrogens from either a clinical or laboratory standpoint. It is the clinical effects which chiefly concern the practitioner who treats such conditions as vasomotor menopausal symptoms, and it has been amply shown that such manifestations are often relieved by much lower dosage than is necessary to produce full vaginal cornification. In other words, there appears to be no parallelism between the clinical response and the vaginal reaction. Any of the estrogens is likely to be effective if used in adequate dosage, although they of course vary in their degree of estrogenic potency, milligram for milligram. But the practitioner can soon become familiar with a few standard preparations and learn to use them intelligently.—Ed.)

THE CONTROL OF OVARIAN ACTIVITY

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West. J. Surg., 56: 451-454 (Aug.) 1948

There are a number of hormones which are concerned directly or indirectly with the control of ovarian activity, but this discussion covers only the role of the gonadotrophic hormones. The evidence points conclusively to the view that there are several gonadotrophins which can be distinguished by chemical and biological means. However, it is the author's belief that these hormones as extracted represent breakdown products from a single mother gonadotrophin in the pituitary, and recent experimental evidence seems to substantiate this view. In addition to the gonadotrophin of pituitary origin, chorionic gonadotrophin and equine gonadotrophin show a distinct effect on ovarian activity.

In the immature female rat the gonadotrophic response varies with the age of the rat and dose of the hormone. If one or two I.U. of this hormone are adminis-

reported by the authors, will seem to many to be a bit too "pat," as exceptions would certainly be expected.

While it is probably true that vaginal smears may be helpful in differentiating the symptoms of the menopause from those of a psychoneurosis, in the comparatively rare case in which a wise clinical evaluation does not make this possible, I do not believe that vaginal smears are any longer regarded, as they once were, as an important guide to dosage for vasomotor menopausal symptoms. The reason for this is that it has been abundantly shown that the vasomotor symptoms are often completely relieved by doses much smaller than those required to bring about full cornification of the vaginal epithelium.

Again, I do not believe that most surgeons would resort to vaginal smears in deciding on whether or not to conserve the adnexa, nor do I think that many will agree that "the diagnosis of malignancy is possible by vaginal smear in almost 100 per cent of cases." The soundest and most experienced cytologists urge that the finding of malignant cells is to be considered supplementary and preliminary to the more decisive method of biopsy, and that the chief value of the smear technic is as a screening method. Although one does not get that impression from the abstract, it is possible that this is what the authors really mean. —Ed.)

THE MENSTRUAL CYCLE

PRACTICAL APPLICATION OF VAGINAL SMEAR AS A METHOD IN CLINICAL GYNECOLOGY

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Delaware State M. J., 20: 109-113 (June) 1948

The authors have studied the vaginal cytology in over 500 cases and have found it of value in a wide variety of conditions. It was utilized in the diagnosis of endocrine states. Ovulation smears were found on the seventh to twentieth day after menstruation. Atrophic smears were found at the menopause and in cases of amenorrhea and hypomenorrhea. Hyperestrogen smears were commonly found in patients with functional bleeding.

The most important use of the vaginal smear in respect to treatment is its application to menopausal therapy. Overdosage with estrogen can be prevented by serial studies of the vaginal smears and true menopausal syndrome can be differentiated from psychoneurosis. Patients whose symptoms continue in spite of a saturated estrogen smear must be considered as psychoneurotic. It was also shown that certain estrogen deficiency states show an improvement in smears following the administration of thyroid extract.

Definite changes have been noted in the vaginal smear during pregnancy which are characterized by groups of cells of the basophilic intermediate type and basophilic superficial type occurring in dense clumps. On occasion, the smear may be of value in the diagnosis of pregnancy. Aberrations from the normal pregnancy smear are seen in abortions and ectopic pregnancies, in which cases the acidophilic cells usually predominate.

Occasionally, the knowledge gained by vaginal smear will influence surgical judgment, especially in the problem of conservation of the adnexa in women past 40 years of age. Menopausal smears do not always appear atrophic, and in such cases conservation of the adnexa seems wise.

In suspected cases, the diagnosis of malignancy was possible by vaginal smear in almost 100 per cent of cases. In general, all malignant cells have certain common characteristics. They usually occur in clusters, are unequal in size, shape and staining reaction. The nucleus is often large, irregular or fragmented, and the chromatin is distributed in clumps or strands. Nucleoli and mitosis may or may not be seen. 10 figures.

(This report impresses me as being a rather over-enthusiastic one as regards the value of vaginal cytology in the diagnosis of endocrine states. There are certainly simpler and more reliable ways of determining ovulation than through the use of smears. The smear findings at the menopause, in amenorrhea and hypomenorrhea, and also in functional bleeding, as

mous" he means to refer to the so-called spinal cell growths, which make up a far larger proportion of epidermoid tumors than the basal cell variety.

He speaks of 75 patients in clinical Stages I, II and III who underwent radical operation, and suggested that in his Clinic the radical surgical plan has been far more widely applied than in most others. The indications for this surgical plan, in those clinics in which it is being applied, are far more restricted, being usually limited to Stage I and perhaps also some Stage II cases. The as yet incomplete statistics reported by Ross do not appear very hopeful. He very properly calls attention to the frequent and at times serious sequelae which may follow X-ray therapy.—Ed.)

PRIMARY MELANOMA OF THE VAGINA WITH A REVIEW OF THE LITERATURE

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AND R. G. LIVINGSTONE, BOSTON, MASS.

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Am. J. Obst. & Gynec., 56: 325-334, 1948

The case presented is that of a 28-year-old white female who was first seen with the complaints of a persistent yellow vaginal discharge, occasionally streaked with blood, and painful coitus of 10 months' duration. Examination revealed a rounded, flat, non-pigmented tumor, about 2 cm. in diameter, within the vaginal introitus on the middle part of the left lateral wall. This tumor was excised and the pathological report was that the growth was benign. Approximately 2½ years later a recurrence was found just anterior to the old operative scar. Excision was again performed and on this occasion histopathological study revealed a melanoma. A radical dissection of the regional gland was performed in combination with vulvectomy. The post-operative course was satisfactory except for the occurrence of several small areas of skin necrosis which required further surgical treatment. Microscopic examination of the regional glands and the remainder of the vulva showed no metastatic lesion. The patient returned to normal active life, including normal coitus, and is free of recurrence 18 months following operation.

A group of 17 previously recorded cases is reviewed and an account of the development and course of the disease is briefly given. 5 figures.

(Primary melanoma of the vagina is an exceedingly rare lesion, and, so far as I know, no instance of it has been observed in the more than 80,000 cases which have passed through the Laboratory of Gynecological Pathology at the Johns Hopkins Medical School. The paper abstracted above presents a good summary of the literature of the subject. There is still some uncertainty as to the exact histogenesis of this tumor, although pathologists have apparently pretty well agreed that it is of epithelial type, and that the name melanoma is to be preferred to the older one of melanosarcoma. Pack, whose experience with tumors of this group is probably greater than that of anyone else, has urged that the simple wide local excision formerly practiced for the treatment of these tumors is inadequate and that

VULVA AND VAGINA

GENITAL MALIGNANCY IN THE FEMALE

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South. Surg., 14: 651-658 (Sept.) 1948

The author feels that the mortality rate in genital malignancy, although improved in recent years, still leaves much to be desired. Early diagnosis is essential for prompt treatment of these tumors, and it is an absolute necessity to have multiple procedures to establish or rule out malignancy. In a series of 2353 cases in 1947, malignancy was found in 151 cases. There was a failure of diagnosis by smear alone in 8.6 per cent of these cases. In 1.5 per cent of the cases, a false positive diagnosis of malignancy was made by smear.

Carcinoma of the vulva was found in 57 patients in a review of the records at Duke University Hospital. Fifty-three were squamous cell and 4 basal cell carcinomas. The salvage rate was 33 per cent. Treatment of choice was x-ray followed by radical vulvectomy and groin dissection. From 1944 to 1947, 530 new patients with carcinoma of the cervix were treated. Because of the poor recovery rate with this type of lesion, it was decided to resort to a radical hysterectomy, bilateral salpingo-oophorectomy, excision of a large part of the vagina, dissection of the ureters and ureteral, obturator and iliac nodes together with the fat. With this procedure the morbidity rate was high and 9 patients developed fistulae. There was no operative mortality, but of 75 patients in clinical stages I, II and III who underwent this operation, 5 died within 10 to 16 months and 15 additional patients are known to have metastases. Treatment of fundal and ovarian carcinoma requires individualization in every case. However, as a general rule, the author prefers the combination of radium and surgery in the treatment of fundal malignancy. He draws attention to the increased incidence of ovarian malignancies, and in such cases operation is imperative. Roentgen therapy alone has proved disappointing in these conditions.

X-ray treatment may be a two-edged sword and the complications of such therapy may be more distressing to the patient than the original lesion. Some of the complications commonly encountered are: erythema, tanning, telangiectasia and even ulceration of the skin; leukopenia; vaginitis; stenosis of the vaginal canal; intestinal stenosis, stricture, hemorrhage and fistula formation; intestinal and rectal irritation; and pyometra. The majority of these unpleasant side effects may be avoided by careful selection of the patients, careful preparation of the patient and careful treatment and follow-up.

(An excellent short, panoramic review of a very wide field. In the group of vulvar carcinomas, the author differentiates between squamous and basal cell carcinomas, although basal cell tumors belong to the squamous or epidermoid cancers. I suspect that by "squa-

ease of administration, the ability to treat ambulatory patients and the factor of self-administration as advantages of this method.

A CASE OF PARTIAL ATRESIA OF THE VAGINA

G. B. THOMAS

J. Obst. & Gynaec. Brit. Emp., 55: 149-151 (April) 1948

The writer describes his technic employed to establish a lower vagina in a 17-year-old Hindu girl who had normally developed ovaries, tubes and uterus. The patient had had no periods nor any pain suggesting cryptomenorrhea. Secondary sexual characteristics were well marked and examination was negative except that beyond the urethra there was an expanse of vulval skin reaching to the perineum. Rectally, a soft boggy swelling could just be reached by the examining finger.

Under spinal analgesia, an index finger was placed in the rectum and a metal catheter was held in the urethra and bladder. A transverse incision was then made where the vulval skin met the perineal. A track was then easily established between the rectum and bladder for some 3 to 3½ inches, until the swelling previously detected per rectum was reached. The abdomen was then opened, the peritoneum of the uterovesical pouch incised, and when the bladder had been pushed away from the cervix, the lowermost part of the hematocolpos could be reached. An assistant pushed 2 fingers into the space previously dissected from the perineum and the fascia separating them from above was cut. A transverse incision was then made low along the antero-inferior aspect of the hematocolpos, enlarging it to 1½ inches. Traction sutures were passed through the lips of this incision and down through the track. These were used to pull the vagina through and down toward the perineum. The lips of the vaginal incision were sutured to the perineal incision. Examination per vaginam was now easy with 2 fingers and the anatomy felt normal.

About 3 weeks postoperatively, one finger could be inserted into the vagina with ease and 2 fingers with slight difficulty. A Sims's speculum could be introduced easily and the cervix seen. A normal and painless period occurred about 5 weeks postoperatively.

(In spite of the absence of menstrual molimina, this patient obviously had a cryptomenorrhea, as the author later speaks of a hematocolpos, which had produced the "soft boggy swelling" noted on rectal examination. The atresia presumably involved the lower portion of the vagina rather than being of the more common type of imperforate hymen. It is sometimes difficult to evaluate the exact status from a written description, but, since the cervix evidently communicated normally with the upper portion of the vagina, one wonders why it was necessary to open the abdomen, and why the patency of the vaginal canal could not have been restored by a colpoplastic procedure from below.—Ed.)

wide extirpation of the regional lymph structures is advisable. When the tumor is vaginal it can be seen that this plan means a very formidable procedure, including not only removal of as much vagina as possible, but also vulvectomy and the excision of all the lymph glands embraced in the Basset type of operation for vulvar carcinoma.—Ed.)

PENICILLIN ADMINISTRATION VIA THE VAGINA

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New York State J. M., 48: 1159-1161, 1948

Five cases demonstrating the clinical application of penicillin calcium in cocoa butter suppositories administered vaginally are reported. All cases were hospitalized. The suppositories used in treatment contained 100,000 units of penicillin.

Case 1 was a patient with induced abortion 5 months previously. The diagnosis was acute bilateral salpingo-oophoritis with pelvic peritonitis, cause undetermined. Two suppositories were given every 2 hours for 30 doses, followed by 2 suppositories every 4 hours for 4 doses. The total dosage was 6,800,000 units and the duration of treatment was 5 days. At the 28th dose the blood level of penicillin was 1.3 units per cc. The final examination at the time of discharge showed a normal pelvis.

Case 2 was a 22-year-old nulligravida with a clinical diagnosis of acute specific cervicitis and bilateral salpingo-oophoritis. Two vaginal suppositories every 4 hours for 18 doses followed by one every 4 hours for 4 doses, with a total dosage of 4,200,000 units, were administered. Pelvic examination after 4 days revealed normal findings to palpation.

Case 3 complained of abdominal pain, fever and a sanguinous vaginal discharge. A cervical smear was positive for gonococci. One penicillin suppository was administered every 2 hours for 17 doses. A cervical smear was negative after 24 hours.

Smear and culture of the cervix and urethra were positive for gonococci in case 4. The diagnosis was acute specific urethritis, cervicitis and salpingitis. Twenty-two single suppositories were given at 4-hour intervals. Smear and culture were negative after 48 hours.

The last case was diagnosed as acute cystitis. A total of 2,800,000 units of penicillin was given by vaginal suppositories over a period of 48 hours. Symptoms subsided within 24 hours.

The 5 patients presented in this paper were treated for gonococcal and streptococcal infections by intravaginal calcium penicillin suppositories and the therapeutic results paralleled those obtained with intramuscular penicillin. However, the authors feel that the efficiency of this method as compared with oral or intramuscular methods has not been accurately established. They point out the

3 days previously and was followed by bleeding. Treatment consisted of transfusion, bed rest and hot douches.

A review of 133 cases of major vaginal tears resulting from coitus is made.

(The 3 cases of serious coital injury reported in the 2 preceding abstracts are surprisingly similar, and they emphasize that coital injury is not by any means limited to the region of the introitus and perineum. The lacerations, sometimes extensive, of the orificial area are the type most likely to occur with the first coitus, but it is of interest that many of the deeper vaginal injuries, such as those reported above, have been noted in experienced practitioners of the art. The numerous reports of similar nature reported in the literature suggest that coitus may be a dangerous pastime, and that it is the woman who usually pays. I do not recall having ever seen a report of any serious coital trauma to the male.—Ed.)

A LARGE FIBROMYXOMA OF THE VULVA

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J. Obst. & Gynaec. Brit. Emp., 55: 334-335 (June) 1948

The patient whose case is presented in this paper was 42 years old, had had 2 children and 2 abortions, and complained of a large, soft and diffuse swelling of the left labium majus; this had been incised on 2 occasions in the previous 8 years. At operation, after the incision had been made, a lobulated, soft and pinkish mass presented. This occupied not only the entire left labium but also extended high into the ischio-rectal fossa on the same side. The mass was dissected out completely and was the size of a melon. Grossly, the tumor contained small cystic spaces and microscopically, it consisted of stellate cells in a fibromyxomatous matrix. There was no histological evidence of malignancy.

(While a tumor the size of a melon is "some pumpkins" (no pun intended), it is of definitely lower size-caste than the famous vulvar fibroma reported by Buckner in 1851. The daguerrotype which he had made has been widely copied in textbooks. It shows the woman straddling her tumor much as she would a horse. It weighed 264 pounds. Like many other large fibromas of the vulva, it really arose from the intrapelvic connective tissue, its growth extending through the inguinal canal to the vulva. It may be recalled that Buckner relates that he did not see the patient until her death, when he was called in to whittle her down so that she could be fitted into a coffin.—Ed.)

VAGINAL INJURY AT COITUS

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Brit. Med. J. 2: 226-227, July 24, 1948

A case of injury to the vaginal vault during normal coitus is presented. The patient, a well developed female of 17½ years, para I and 3½ months postpartum, complained of severe vaginal hemorrhage and lower abdominal pain following intercourse. Examination revealed a firm, closed cervix and no signs of pregnancy. Inspection with a speculum showed a linear laceration 5 cm. long high in the vaginal vault and extending from one lateral fornix to another across the vault. The laceration was composed of vascular cellular tissue and the peritoneum was not visible. The edges of the tear were co-opted with interrupted sutures and the hemorrhage was arrested. The area was sprayed with penicillin powder and the patient made an uneventful recovery.

Since intercourse was apparently normal and without any disproportion in size of either partner, attention is called to the part that the recent pregnancy may have played in softening and vascularizing the parts. Several other cases of such injury during the postpartum months are mentioned. Good surgical repair is recommended as the hemorrhage may actually threaten life.

(See comment on following abstract of paper by Diddle.—Ed.)

RUPTURE OF THE VAGINAL VAULT DURING COITUS

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West. J. Surg., 56: 414-416 (July) 1948

Two cases of rupture of the vaginal vault during intercourse are reported. The first patient, 19 years old and 2 months postpartum, was admitted with moderately severe vaginal bleeding. Inspection of the vaginal apex revealed a 4 cm. tear involving the entire thickness of the vaginal wall. It was ascertained that violent sexual intercourse was consummated in a half sitting position four hours before admission. This was followed by sharp pain and bleeding. Treatment included ferrous sulfate and blood transfusion. Bleeding ceased after 24 hours.

The second case was a 21-year-old female 16 days postpartum who complained of vaginal bleeding. A gaping tear covered by friable granulation tissue was found across the posterior and left lateral fornix. Intercourse had taken place

THE UTERUS

RECTAL INJURIES FOLLOWING RADIUM TREATMENT OF CANCER OF THE CERVIX UTERI

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Acta radiol., Supplement 64, 1947

During the last few years a type of intestinal injuries has been observed in America which consists chiefly of intestinal strictures, because of the shift toward a very intensive roentgen treatment, using high voltage, and sometimes also super voltage. In Sweden the treatment of uterine cancer was, almost from the beginning, performed along the lines of the technique now known as the *Stockholm-method*, further developed by Heyman. In using this method the injuries encountered are almost exclusively localized to the rectum. The incidence of rectal injuries following the modern irradiation treatment of uterine cancer varies greatly in different clinics. It may be assumed, however, that a rectal reaction will invariably occur in 5 to 10 per cent of the patients of a large material, treated with a sufficiently large dosage to ensure a satisfactory cure of the cancer.

The primary object of the present investigation is to study the pathogenesis of the rectal radiation injury and its influence upon the healing process. A series of 3392 cases of cancer of the cervix uteri, treated at Radiumhemmet from 1914 to 1937 has been analyzed in detail. The number of rectal reactions during this time amounted to 313, corresponding to an incidence of 9.2 per cent. In this compilation all cases where the patient has suffered from rectal disturbances following the treatment, or such where alterations of the rectum have been demonstrated by palpation are included, as are also 28 cases that have exhibited only subjective symptoms, but where digital examination of the rectum failed to reveal any pathologic changes. On the other hand, 24 cases are included that showed no symptoms, but in which digital examination of the rectum revealed typical radiation changes. Also included are 20 cases in which the cancer involved the intestine, but in which a simultaneous radiation injury could not be ruled out. The control group in this study comprises all patients whose surnames begin with A, B or R, plus so many consecutively from the registration with names beginning with S that a total number of 313 was obtained. The control patients were included only if they had been followed up for at least one year, and showed no signs of rectal injuries.

The *Stockholm-method* of treatment is a fractionated contact treatment in which the filtration is equivalent to 3 mm. of lead. A typical treatment series according to the method would be:

In the uterus 40 mg. el. x 20 hrs. 800 mg. el. hrs.

In the vagina 75 mg. el. x 20 hrs. 1500 mg. el. hrs.

ATABRINE IN THE TREATMENT OF TRICHOMONAS VAGINITIS

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North Carolina M. J., 9: 309 (June) 1948

Six cases of trichomonas vaginitis have been treated with 4 insufflations of atabrine (30 grains) in finely powdered boric acid (one ounce) at 2-day intervals. All of these cases had been resistant to all other forms of therapy. In one case treatment was stopped because of a chemical vaginitis after the second insufflation. All cases, including the one which developed the chemical vaginitis, showed clinical improvement and smears were negative after the completion of therapy. No systemic reactions were encountered. The author believes that routine use of atabrine may prove of value in the treatment of trichomonas vaginitis.

(No one can complain of any paucity of methods of treating trichomonas vaginitis, but there is still room for improvement. I do not know enough about chemistry to know whether the use of atabrine seems rational and whether it will prove to be of any value or whether it will be just "another one of those things."—Ed.)

to generation of such. In the vessel walls, which in the earlier stages are edematous, hyalinization and sclerosis take place. The endangitis often leads to thrombosis. In the rectum the sclerosis is most pronounced in the veins and diminishes toward the serosa. Telangiectasias appear and often constitute an essential part of the histologic picture. In the hyalinized and sclerotic connective tissue irregular and swollen muscle fibers are found mixed with some showing atrophy and degeneration. The degenerative changes also affect the ganglia cells. The cells of the connective tissue are partly swollen. The cell nuclei are in considerable part irregularly formed and a moderate polymorphism of the cells and nuclei is found. If the lesion leads to necrosis, sharply delimited ulcers with a yellow-white coat and pronounced ridge-like edges develop. In the bottom of the ulcer there is a marked infiltration of leucocytes and plasma cells which, together with granulation tissue, penetrate the muscular coat, splitting it. On healing of the lesion an atrophic scar develops, covered by a thin mucous membrane which is very easily injured if the intestinal contents are solid. Numerous telangiectasias are generally found in the surrounding tissues.

In regard to pathogenesis, the author discusses several questions, drawing upon investigations at Radiumhemmet for his answers. The problems considered are as follows.

1. *How has the dosage influenced the production of rectal injuries?*

During the autumn of 1931 and the winter of 1932 a series of measurements was performed by the physical laboratory at Radiumhemmet of the radiation intensity in the rectum during the treatment of 109 cases of uterine carcinoma. The author has reviewed 17 of these cases which complied with the necessary criteria in order to find out whether any conclusions could be drawn as to the radium dose necessary to produce a rectal reaction when employing the *Stockholm-method*. From his investigations, the following facts became evident:

1. The scar of the rectal lesions corresponds well to the site of the maximum dose.

2. The cases with the greatest dose have presented rectal disorders.

3. When the different diagrams relating to data on this aspect have been transposed so that the maxima coincide, all cases where the maximal dose registered superseded 400 Imc. hrs. presented rectal disorders, whereas only one of the 12 cases which received less than 400 Imc. hrs. had a rectal reaction.

4. The dosage expressed in mg. el. hrs. has in general been uniform.

Therefore one is probably justified in assuming that the limit for the production of a rectal reaction, when employing the modified *Stockholm-method*, lies at a total dose of approximately 400 Imc. hrs. (appr. 3300 r units). One must bear in mind, however, that this value corresponds to the dose at a distance of 7 mms. from the mucosal surface itself, the rubber tube having a wall thickness of about 2 mms., and the condenser chambers a radius of 5 mm. The dose in the most sensitive layer of the mucosa, the vascular layer, which is located about 2 mms. beneath the mucosal surface, must therefore have been correspondingly greater.

The great doses have more often been administered on a small area in the rectal injury series than in the control series, in which latter case this relation has been

The treatment is repeated 3 times with a week's interval between the first and second treatment, and 3 weeks between the second and third. The total duration of radium application is about 60 hours. The total dose in these similar treatments amounts to 2400 mg. el. hrs. in the uterus and 4500 mg. el. hrs. in the vagina. In the case of rectal injuries 2 treatments have been administered in 62 per cent, 3 in 33 per cent and more than 3 in 4 per cent of the cases, while in one per cent only one treatment was given. In the control series 2 treatments have been administered in 65 per cent, 3 treatments in 31 per cent, and more than 3 treatments in 4 per cent of the cases. Since 1929 all cases have received supplementary radiation treatment 3 weeks after the last radium application. The roentgen skin dosage has been $3 \times \frac{1}{3}$ SED on each parametrium through 2 abdominal portals, and in some advanced cases an additional application of the same dose through one or 2 sacroiliac portals. Since the introduction of the dosage unit r, a dose of 3×400 r has been applied to each parametrium using a compression tube.

In rectal injuries an initial proctitis, lasting a week or 2, is observed in 31 per cent of patients, early reaction. The time of appearance of the late reaction varies. In 92 per cent of cases it became evident within a year after treatment, and in 60 per cent within the first 8 months. In 69 per cent of cases a late reaction occurred without an initial proctitis. The clinical picture presenting tenesmus, discharge of mucus and hemorrhage, is the same as that of ordinary proctitis, but the development of symptoms in a patient subjected to radium treatment within the last year is characteristic. The typical lesion consists of a readily bleeding local swelling of the mucosa of the anterior wall of the rectum at the level of the vaginal vault. Eventually a circumscribed ulcer may develop here, finally resulting in a scar surrounded by telangiectasias and often located on a mucosal fold protruding into the lumen. In the later stages a swelling of the parametria generally develops, forming a transverse cord which reaches the pelvic wall on one or both sides.

According to the author's experience at Radiumhemmet, the lesions may be classified as follows:

	<i>No. of cases</i>	<i>Per cent of all cases treated</i>
Subjective symptoms only.....	28	0.8
Slight local lesions.....	178	5.2
Ulceration.....	91	2.7
Rectovaginal fistulas.....	16	0.5
	<u>313</u>	<u>9.2</u>

The writer describes the pathological anatomy of these lesions. In the earliest stages the mucosa presents a glassy aspect. Numerous inclusions of mucus can be seen in the epithelial cells and a hypersecretion of mucus takes place. All the coats are edematous. The cell nuclei swell, presenting atypical shapes with nucleoli of highly transformed appearance. The muscle fibers are vacuolized; sometimes a degeneration similar to that of Zenker develops. Later, the changes in the vessels and the connective tissue dominate. The amount of collagen increases and a hyalinization of the same takes place. The appearance of the collagen in sections is, however, mostly due to the swelling of the fibers and not

should avoid capsules as far as possible, as these produce greater radiation intensity in the rectum as per mg. of radium, than when employing boxes. It is perhaps also possible to increase the intrauterine dose in suitable cases and to decrease the vaginal one in the same degree.

In treatment of rectal injuries, one must above all avoid further radiation treatment. The symptoms of proctitis respond favorably to small, warm enemas of sodium chloride solution, olive oil or lightly astringent solutions. If stenosis occurs, one can try to counteract the shrinking by repeated dilatations with Hegar dilators. If the stenosis becomes too great or the rectal symptoms too incapacitating one may be compelled to perform a colostomy that can generally be closed later on. Patients should be instructed to avoid constipation by suitable diet.

Finally, the author investigates the factors influencing the cure rate in cases with rectal injury. The 5-year cures among the 313 cases with rectal reaction in the material from Radiumhemmet amount to 49.5 per cent \pm 2.8 per cent (155 cases), and among the remaining 3079 cases it reaches only 24.0 per cent \pm 0.8 per cent (738 cases). This represents a considerable and statistically established difference, and also agrees with clinical experience.

One cause of the greater cure rate in cases with rectal injury is the fact that some of the most advanced cases die before having developed any symptoms of rectal injury, thus eluding the statistics. However, it is shown that this possible error in time factor cannot by itself explain the increased cure rate.

It is found that the series of rectal injury cases and the control material present an almost identical distribution of the different stages of carcinoma of the cervix. Thus the difference between them in cure rate cannot depend on this factor.

A second cause of the increased cure rate is the size of the tumor. The tumor sizes estimated on rectal palpation, as made by the same person in nearly all cases, are graded from size 1 to size 3, in order of small to larger. Tumors of size 1 are found in 52 per cent, and of sizes 2 and 3 in 24 per cent, respectively, of the cases presenting rectal injury. The corresponding figures for the control material are 33.2 per cent, 25.2 per cent and 41.6 per cent, respectively. Thus the rectal injury series contains a considerably greater number of small tumors and a smaller number of large tumors, than the control series. The differences are statistically established. The 5-year cure rate depends on the size of the tumor and diminishes with increasing size in both series.

A third, and probably one of the chief causes of the greater 5-year cure rate among the cases with rectal injury is the dose administered as per volume unit of tumor. With increased dosage there seems to be an increased 5-year cure rate. The dosage per c. cm. of tumor has been much greater in the rectal injury series than in the control series. Thus, the highest dose among the control cases is only 126 mg. el. hrs. per c. cm. of tumor, whereas the lowest dose among the rectal injury series is 149 mg. el. hrs. per c. cm. of tumor.

The author concludes that the production of a rectal injury in a given case may be prevented by taking the above mentioned predisposing factors into consideration when calculating the dose. One must, however, endeavor to attain

more favorable. The difference is statistically established both as regards tumor area 1 and tumor area 3.

The investigation shows that if one surpasses the usual dosage in mg. el. hrs. of the *Stockholm-method*, one must count with an increased risk of producing a rectal lesion. When applying the usual dose, the production of a rectal lesion primarily depends on the concentration of radium per area unit.

In regard to the usual supplementary roentgen treatment employed during the years 1929 to 1937 with a total rectal dosage of approximately 300 r, this has probably not influenced the production of the rectal lesions to any great extent, this being in concordance with the clinical findings. In the isolated cases, however, where the patient received additional treatment from either of the gluteal regions, one must consider that the roentgen treatment has contributed to the production of the rectal lesion.

2. *Are there any individually predisposing factors?*

In the control group, 47 per cent ± 2.8 per cent of the patients are above 50 years of age, whereas in the group presenting rectal injuries 65.5 per cent ± 2.7 per cent are above 50, the difference thus being statistically established. The same result is obtained when comparing with all 3079 cases without rectal injury. Thus there seems to be an increasing disposition for radiation injuries in the rectum with increasing age.

Among the cases with rectal reaction, 4.8 per cent ± 1.2 per cent had previously suffered from syphilis, and 10 of these 15 patients had a positive Wassermann reaction at the time of treatment. In the control group, syphilitic infection was present in 6 cases, or 1.9 per cent ± 0.8 per cent. Although the difference is not statistically established, the figures suggest that syphilitic infection favors the production of rectal injuries.

It is found that tumors protruding into the vagina are present in 36.7 per cent ± 2.7 per cent in the rectal injury series, whereas the corresponding figure in the control series amounts to 50.8 per cent ± 2.8 per cent. It therefore seems that a tumor protruding into the vaginal lumen lessens the danger of a rectal reaction, probably because it separates the vaginal radium applicators, thereby diminishing the radiation intensity to the rectum.

3. *Other factors predisposing to a rectal injury.*

As vaginal applicators, both flat applicators (boxes) and capsules have been used. In the cases with rectal injuries, only capsules have been used in 67.3 per cent ± 2.7 per cent, and boxes only in 9.9 per cent ± 1.7 per cent. The corresponding figures in the control material are 32.0 per cent ± 2.6 per cent and 35.8 per cent ± 2.7 per cent, respectively. The yearly percentage of rectal injuries presents a certain parallelism to the percentage of cases treated with vaginal capsules only. Thus the use of capsule shaped vaginal applicators must be considered as an essential cause of the rectal injuries.

As to prophylaxis, the author's personal opinion is that the most important single factor is to avoid overdosage. The dose must be calculated with special care in syphilitic cases and in cases of advanced age, as well as in cases with a narrow vagina. When electing vaginal applicators in the *Stockholm-method* one

mined by response to irradiation and operability. Of the cases observed for a period of 3 years or longer, 67.4 per cent are alive and free of disease. This figure compares favorably with the cure rate by surgery alone, which has been reported in 50 to 55 per cent of 5-year cures. It also parallels the cure rate of the larger series of Heyman, also treated by irradiation.

The packing method has proved itself to be an important advance in radiation technique for the treatment of corpus cancer. Results proved to be so satisfactory that surgery was used only after the failure of irradiation. However, the combination of both of these forms of treatment is practiced by most gynecologists today.

(The authors' views will probably be looked upon by many readers as reactionary in that they advocate surgery only "after the failure of irradiation." It is true that, as they say, Heyman and a number of others did, a good many years ago, treat considerable groups of patients with radiotherapy alone, being apparently influenced by the fact that in the management of cervical cancer the results after radiotherapy were about as good as with surgery in the operable group, with far less primary mortality. But surgery for cervical cancer is a far more formidable procedure than it is for endometrial carcinoma, while on the other hand the intracavitary use of radium for the latter has always presented troublesome problems as to technics.

Be that as it may, the accumulating reports from various clinics have indicated an incidence of something like 50 per cent of residual cancer, on the basis of histological study of uteri removed after radiation. Opinion is now quite well crystallized to the effect that hysterectomy should be an essential part of the treatment of endometrial carcinoma, except of course those in which surgery is contraindicated by such factors as a very far advanced stage of the disease, serious debility or serious organic disease, or extreme obesity.

On the other hand, the view now prevails that radiation as a preliminary to operation probably yields better results than either operation alone or radiotherapy alone, although it cannot be said that statistics on this point are yet impressive in the numbers of follow-up studies made. The destructive or devitalizing effects upon the intrauterine cancer, the sterilization of the local cancer area, the fibrotic entrapment of cancer cells—all these are urged as advantages, whether radium or x-ray be chosen for the preliminary radiation. Another advantage claimed is that this plan greatly lessens the hazard of disseminating cancer cells at operation.

Not all surgeons are convinced of the advantage of preliminary radiation, especially in the relatively early group, and a number of papers have appeared rebelling against the prevailing fashion. I myself do not always employ preliminary radiation, as I have previously discussed in these pages. Like other aspects of cancer therapy, a considerable time span is necessary for intelligent evaluation of different plans, and we shall have to wait and see.—Ed.)

the maximum tolerable dose, without damaging the adjacent tissues, as there seems to be a parallelism between the dosage per volume unit of tumor and the 5-year cure rate in the examined material, showing that greater cure rate is obtained with increasing dosage. The investigation thus points toward the fact that better cure rates could probably be obtained by increased individualization of treatment, taking the size of the tumor into special consideration. 19 figures.

(This paper has been abstracted at considerable length because it represents the most complete study of the subject with which I am familiar. The original paper is in the form of a monograph which, with its complete bibliography of the subject, comprises 79 pages. It is based upon the large material of the Radium-hemmet, which has contributed so richly to the development of radiotherapy in uterine cancer.

There have been many previous publications dealing with intestinal lesions produced by radiation therapy, but for the most part these have dealt largely with their clinical aspects. The present study, however, correlates these clinical manifestations with histological investigations of the lesions as well as with the dosages and technics employed, predisposing factors, prophylaxis, etc.

While the minor forms of rectal irritation and proctitis do not present such serious problems, anyone who has seen cases of the severe so-called factitious proctitis can appreciate that the patient's suffering may be as great or greater than with the original cancer. Even colostomy may at times be necessary to alleviate the patient's suffering or to lessen the severity of the bleeding which sometimes occurs. The author has no new suggestions as to the management of these troublesome cases, but his paper is commended to the attention of all those interested in the radiological therapy of cervical cancer.—Ed.)

THE RADIATION TREATMENT OF CARCINOMA OF THE CORPUS UTERI

ETHLYN TRAPP AND MARGARET HARDIE

British Columbia Cancer Institute, Vancouver, B.C.

Canad. M. A. J., 58: 115-118, 1948

Until fairly recently cancer of the corpus uteri has been considered primarily a surgical disease. However, there is a small group of anaplastic tumors that respond poorly to surgery alone, which led to the employment of irradiation therapy. Heyman, one of the pioneers of radiation therapy, developed the multiple source method of treatment, and this has been found to be more effectual than the tandem application in reducing the amount of residual tumor.

The authors have used the method of multiple applicators packed into the uterine cavity in the treatment of 59 cases of carcinoma of the uterine body. Two courses of treatment were given at a 3-week interval with a total irradiation of 3000-6000 mgm. hours. In most cases intracavitary radium was combined with deep x-ray therapy. The primary treatment in these 59 cases fell into the following groups: 6 were treated by radium alone; 47 by radium and x-ray; and 6 by radium, x-ray and surgery. The course of treatment in each case was deter-

A CASE OF TUBERCULOSIS OF THE CERVIX WHICH
MACROSCOPICALLY RESEMBLED CARCINOMA
OF THE CERVIX

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Liverpool, England

J. Obst. & Gynaec. Brit. Emp., 55: 336-337 (June) 1948

A 24-year-old nulliparous patient is presented who complained of amenorrhea and a brown vaginal discharge of 18 months' duration. She had previously had a dilatation and curettage which had been followed by 2 normal periods and then return of amenorrhea. She also gave a history of an attack of hematuria 2 months prior to hospitalization. The cervix was seen to be the site of a hypertrophic growth which bled on being touched and which presented the typical malignant picture. A biopsy of the cervix and endometrium revealed tuberculosis. In the absence of evidence of urinary or other extragenital tuberculosis, the whole of the uterus and both appendages, which were the seat of caseous tubo-ovarian abscesses, were removed. One of the abscesses broke at operation and a sinus tract persisted for 5 months before closing after a course of small doses of deep x-ray therapy.

The author emphasizes the value of x-ray therapy as an auxiliary form of treatment in cases of genital tuberculosis, although its exact mode of action is not known. It is pointed out that genital tuberculosis is more common than is generally supposed, and since some cases show a positive Aschheim-Zondek reaction, a diagnosis of pregnancy may be made in error.

(This case shows the value of routine biopsy, even in cases of what appears to be very obvious cancer. In the vast majority of cases the biopsy will be only confirmatory of the clinical impression, but in the rare case it will spring a surprise, revealing tuberculosis or benign condyloma. It is true that the tuberculous nature may sometimes be suspected from the history or from such associated symptom as the hematuria noted in the author's case. Again, the tuberculous cervix will often show a somewhat caseous type of ulceration in association with the hypertrophic change. But the fact remains that mistakes of this sort are sometimes made. In cases of the sort described by the author, the auxiliary value of x-ray therapy commends itself as advisable.—Ed.)

THE TREATMENT OF CARCINOMA OF THE CERVIX UTERI

A. M. EVANS

Vancouver, B. C.

Canad. M. A. J., 59: 458-462 (Nov.) 1948

The author reviews in a general way the natural history of carcinoma of the cervix and discusses in some detail the treatment of carcinoma of the cervix. The literature on this subject includes a variety of procedures in use; however, all the satisfactory methods of treatment apply the same general principles. Surgery for this disease was the earliest form of therapy but is probably only applicable in Stages I and II, a group which makes up a small percentage of all cases seen. Radium treatment as practiced today follows or is a modification of two well-known techniques. The Stockholm technique is essentially one in which relatively large quantities of radium are left in place for 2 or 3 periods of 24 hours each. In the Paris technique, continuous irradiation is provided by smaller quantities of radium left in place several days. X-ray therapy has been used both alone and supplementing the radium therapy. The x-ray field should be directed so that the zone in the midline, to be or already treated, receives no irradiation. Most authorities also agree that in the presence of pelvic infection, x-ray therapy should be given before radium, and some clinics use it first regardless of the presence of infection. The complications which arise from over-treatment with radium are usually in the rectum, and seldom in the bladder. The type of response to radiation cannot be predicted from a biopsy and every case probably should be treated as though it had already spread beyond the cervix.

At the British Columbia Cancer Institute, treatment given has consisted of radium by a modified Stockholm method and deep x-ray therapy. A total of 5500-8600 mgm. hrs. of radium is given by vaginal and uterine tubes. Deep x-ray is given in doses of 2800-3500 r over a period of about 4 weeks. Four portals are used for the x-ray irradiations. From 1938 to 1947, 338 cases of carcinoma of the cervix have been seen. Eighty-five per cent of the tumors were grades 3 and 4 and 126 cases were available for study of 5-year survivals. A total of 40 cases (31 per cent) showed a 5-year survival with the highest survival rate in the tumors treated while in Stages I and II. 2 figures.

(An excellent short review, stressing the radiotherapeutic management of cancer of the cervix, describing the technic and reporting an over-all salvage rate which compares favorably with that reported from most other clinics.—Ed.)

"MESODERMAL MIXED" TUMOR OF UTERUS

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AND

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J. Obst. & Gynaec. Brit. Emp., 55: 309-311 (June) 1948

The authors review briefly the literature concerning this relatively rare tumor, and point out the variety of opinions which exist concerning the histogenesis and even the classification of this tumor. Many writers on the subject will not accept a tumor as being of this group unless it contains embryonal myoblasts in combination with one or more heterologous elements such as myxomatous tissue, cartilage, glands, etc.

A case is presented of a 73-year-old woman who complained of acute urinary retention and a blood stained vaginal discharge. A mass was felt in the pelvis and the bladder extended up to the umbilicus. A diagnosis of multiple fibroids was made and a panhysterectomy was performed. The postoperative course was uneventful.

On examination of the specimen, the ovary was found to contain a pure fibroma. A ragged mass, 5 by 4 by 1½ inches, was seen in the uterus arising from the region of the internal os. On section of this mass, areas of necrosis and what appeared to be cancellous bone were seen. Histologically, the cells were anaplastic, some of them strap-like and presenting longitudinal and transverse striations. Some areas had the appearance of cartilage.

About 1½ years after the original operation, the patient was seen again complaining of vomiting, abdominal pain and ascites. Nodules were palpated in the abdomen. The patient died shortly thereafter and a partial autopsy showed metastases in the liver, kidney, bowel, pelvis and abdominal wall. Histological examination of the metastatic lesions showed complete anaplasia and no striated cells or cartilage could be identified. 3 figures,

(The rare mixed mesodermal tumors of the uterus are a highly malignant group, and, while they may be looked upon as teratomatous, we can not be sure as to the mechanism of their production. Some have suggested that they arise from müllerian cell rests, but this is improbable in view of the nature of the alien elements, such as striped muscle and cartilage. Others, somewhat more plausibly, suggest that the source of such tumors is mesodermal tissue which is pulled down, as it were, by the wolffian ducts as they descend in the early stages of urogenital embryology. Histologically, and probably histogenetically, they are closely allied to the so-called sarcoma botryoides which occur in the cervix and vaginal vault. In both these tumors striped muscle is a frequent finding, but it is not always easy to recognize, as it is often present in embryonic form.—Ed.)

A CASE OF CARCINOMA OF THE BODY OF THE UTERUS AND FIBROID TREATED WITH RADIUM AND SUBSEQUENTLY BY HYSTERECTOMY

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Manchester, England

J. Obst. & Gynaec. Brit. Emp., 55: 338 (June) 1948

The case is presented of a 60-year-old white woman who had had 3 children and 2 miscarriages, and who was seen with the complaints of "terrible bearing down pains," and a watery discharge with intermittent uterine bleeding. Four months previously she had received radium treatment for carcinoma of the body of the uterus. The uterus was enlarged by fibroids and extended almost to the umbilicus. The uterus and appendages were removed and in addition to the fibroids on the uterus, a large, stinking, necrotic growth was present in its cavity. Four months after operation a presacral neurectomy was carried out because of severe rectal tenesmus. Five years later, the patient was extremely well except that she had acquired the habit of using a rectal suppository of morphia every night.

It was felt that this case should probably have been treated surgically in the first place but it is pointed out that carcinoma of the body of the uterus could be present for many years and yet still remain amenable to surgical treatment. The rectal complication may have been due to the radium slipping out of the uterus into the vaginal cavity. The pain was probably the result of expulsive uterine contractions.

(The author of this paper died only last year, after having served for a comparatively short period as Head of the Manchester Clinic, in which position he had succeeded Sir William Fletcher Shaw, whose publications and whose visits to our country have made his name familiar to American gynecologists. Dougal likewise visited America some years ago as the honor guest of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons. Like Shaw, he was one of the group who established the well-known Manchester operation—Donald, Fothergill, Shaw and Dougal.

The case reported in this paper, which must have been the last or almost the last written by Dougal, presents 2 chief points of interest. First, it shows the frequent inadequacy of radium therapy alone in the cure of endometrial carcinoma, and the wisdom of the modern plan of following the radiotherapy with hysterectomy. The various studies which have been reported of uteri removed after previous irradiation show residual carcinoma still present in something like 50 per cent.

Secondly, the case illustrates that even when the uterus is the seat of a "large, stinking, necrotic growth," evidently of long standing, cure may still follow a radical operation. Nor is the credit for this necessarily to be given to previous radiation. All the older gynecologists will probably recall that long before the days of radium it was frequently noted that even advanced cases, with a history of bleeding perhaps for a couple of years, would sometimes be cured by radical operation, justifying the general feeling that metastasis is likely to occur later in endometrial carcinoma than in the cervical variety.—Ed.)

The author's description of the lymphangiectasis seen in certain uterine myomas is accurate. Minor degrees of such changes are relatively common, but at times the lymphangiectasis is so pronounced that the resulting histological picture may be confusing to one not familiar with it, and may lead to the incorrect diagnosis of lymphangioma. Genuine lymphangioma of the uterus is a rare tumor, and I recall only 3 such cases in my own experience. Similar tumors, also rare, may occur in the ovary. Neoplasms of this purely lymphangiomatous type are benign, but there are cases in which the lymphatic endothelium shows marked overgrowth and invasiveness, and which must be classed as lymphangio-endothelioma, with varying degrees of potential malignancy.

The lesion to which the author refers as "sarcomatoid growth of the endometrial stroma" or "stromal endometriosis" is rare, but it has received considerable attention in the past few years, especially since the publication of the paper of Robertson, Hunter, Larson and Snyder in 1942 (*Am. J. Clin. Path.* 12: 1, 1942). A similar purely stromal type of ovarian endometriosis was described by Casler as far back as 1920. In the uterus the lesion presents the same benign invasion of the musculature which characterizes ordinary adenomyosis, but the invading endometrium is devoid of glands, being made up entirely of stroma.

The malignant prototype, sometimes spoken of as malignant stromatosis, has been described as a separate pathological entity, but this does not seem to me to be justified, because I do not see how it can be separated from endometrial sarcoma. The latter designation refers to sarcoma arising from the endometrial stroma, and this would certainly fit the lesion under discussion.

Curtis' discussion of the so-called luteinomas or adrenal-like tumors of the ovary again emphasizes the meagerness of our knowledge as to their exact nature and histogenesis, and the consequent confusion of nomenclature. Personally, I do not like to see the term luteinoma applied to this group of masculinizing tumors, because I think the morphological resemblance of the constituent cells to lutein cells does not justify the assumption that such tumors are of lutein origin. More often the cells resemble adrenal cells, and there is good reason to believe that at least some of the group are actually of adrenal origin. Other investigators, like Teilum, see a resemblance to the interstitial cells of Leydig, and actually so interpret them. Whether right or wrong, I believe that there is increasing evidence that, since all the gonadal constituents in both sexes are derived from the original gonadal mesenchyme, it is not necessary to invoke an origin from tissues alien to this area in explaining any of the feminizing or masculinizing ovarian tumors—granulosa cell tumors, thecomas, arrhenoblastomas, or the group under immediate discussion, the so-called adrenal tumors or masculinovoblastoma.

In any event, it seems to me to be sensible, for the time being, to avoid the use of the term luteinoma for this neoplastic type, not only for the reasons mentioned above, but also because this term has also been applied, and with much more justification, to tumors of the granulosa or thecomatous type in which complete or almost complete luteinization has taken place. In these there can be no doubt as to the genuinely lutein nature of the cells. In most cases the lutein transformation of the granulosa or thecal cells is morphological and not fully functional, since such tumors, while feminizing, appear to produce only estrogen but not progesterone. In a number of reported cases, however, the lutein cells have produced progesterone, as manifested by the obvious secretory changes seen in the endometrium, even in women long past the menopause.—Ed.)

A CONSIDERATION OF SOME UTERINE AND OVARIAN TUMORS

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West. J. Surg., 56: 404-406 (July) 1948

The author wishes to present ideas concerning the nature and origin of certain pelvic tumors. First of the uterine tumors briefly considered is the lymphangiectatic myoma. Honey combed tumors or tumors with sharply circumscribed cavities with smooth walls are nearly always lymphangiectatic. The spaces are dilated lymph spaces and cysts. They are quite large.

The pathology of the sarcomatoid growth of the endometrial stroma or stromal endometriosis is discussed. Of the 20 cases of this growth reported, 3 or 4 have become sarcomatous and have been fatal. Here the growth apparently develops in the uterus from diffuse stimulation of previously indifferent stromal cells, not from embryonal rests. The tumors pursue a benign, invasive course and are potentially malignant.

A case of a sarcomatous growth of the cervical stroma is described. The patient was a 47-year-old woman in the menopause. Symptoms were annoying discharge, hot flushes and persistent spotting. Examination revealed a large raw cervix, grossly not cancerous. Microscopic sections showed unusual stromal tumor cells, non-malignant but not typical of the cervix. The patient was not seen for one year and returned with a history of daily bloody discharge. Examination showed the cervix 4 times normal in size with a rough, oozing but firm surface. The absence of friability suggested a lesion comparable with a sarcomatoid growth of the endometrium, apparently malignant. Radium irradiation and X-ray therapy reduced the cervix but systemic metastasis by way of the lymphatics and blood stream occurred, resulting in death. Here again is a growth resulting from normal and previously indifferent stromal tissue.

The teratoma of the ovary is composed of embryonic cells and is potentially malignant. One element of this tumor may suppress growth of the others and may give rise to many types of special ovarian tumors.

Two new cases are added to the 15 known cases of luteinoma or so-called adrenal-like tumors. These are nodules of yellow orange color, of walnut size, and are buried in the ovary. They present masculinization symptoms. Microscopic study revealed polyhedral cells or a transition to a stroma of spindle shaped cells. Clearly defined intercellular bridges are seen here. A growth from mature stroma cells is again encountered.

Although evidence warrants acceptance of the belief that these tumors arise from embryonal rests, the author wishes to point out that growth may also arise from normal tissues. They are typically benign and invasive but may become malignant. 2 figures.

(These general comments on certain tumors of the uterus and ovaries are from a well-known gynecologist of many years' experience, and must therefore command attention.

couples, rather than for workers to expect great increases in their salaries or earning capacity as they grow older. The author believes that this financial aid will reduce the incidence of endometriosis as well as the incidence of unhappy and childless marriages.

The symptoms of endometriosis are well known and need no elaboration. The easiest clue to diagnosis on physical examination is a rough, firm and "shotty" feeling behind the cervix which is best felt on rectal examination.

The treatment of endometriosis is clear-cut. Castration will always check the process and is the correct treatment in the older age group, especially if the endometriosis is so severe that it may injure another organ. However, in a young girl who desires children, such radical treatment is to be deplored. It is far better in such a case to resect the bowel or bladder or to resect or transplant the ureter. Resection of ovarian endometriomata and conservation of ovarian tissue is essential in young women. Since the disease progresses slowly, if symptoms should recur, roentgen-ray treatment will stop ovarian function and cause a cessation of growth of the endometriosis.

Endometriosis may be aided by treatment with testosterone or by stilbestrol, but this treatment is not permanent.

The results of conservative treatment are very satisfactory, and re-operation in the author's clinic is indeed rare. In from 9 to 29 per cent of the reported cases a pregnancy has followed conservative surgery. It is important to advise patients to try to become pregnant very soon after conservative operation, when the tubes and ovaries are free.

(The author very properly emphasizes that endometriosis is not always to be viewed with apprehension, and that there are a good many cases in which surgery is not necessary. It should be done, as he says, only for definite indications, although unfortunately these are frequent enough to make surgery for endometriosis fairly common. We all see cases in which endometriosis is undoubtedly present, on the basis of such findings as uterosacral nodules, often combined with adherent and possibly enlarged ovaries, and in which the patient nevertheless has very little discomfort. Since the condition is not a dangerous one, and since it appears to have very little tendency to produce ovarian carcinoma, it can under these circumstances be treated expectantly, just as one does similarly symptomless cases of chronic salpingitis.

On the other hand, there are a good many patients who have such severe dysmenorrhea and not infrequently dyspareunia, that operation is the wise course. It should always be as conservative as possible in the younger group of women in whom later pregnancy is hoped for, especially as in most of them the endometriosis has imposed a high degree of infertility and they have usually been childless. Just why this should be so it is difficult to say, since the tubes are usually patent. There are of course many exceptions, but the incidence of sterility with endometriosis is rather high. The conservative policy in operating on such patients is frequently rewarded, since a good many of them subsequently conceive.

On the other hand, there are cases in which the endometriosis is so widespread, with perhaps endometrial cysts of both ovaries, the uterosacral ligaments, and extensive infiltration of the rectum, sigmoid or bladder that a more radical plan seems the wiser one, as it always is when such patients are approaching middle life. Even in somewhat younger women, I am not sure that most gynecologists would not prefer castration, undesirable though it may be, to such procedures as transplantation of the ureters, as Meigs suggests. Fortunately, such a dilemma is rarely encountered.

ENDOMETRIOSIS

J. V. MEIGS

Boston, Mass.

Ann. Surg., 127: 795-809 (May) 1948

Endometriosis is one of the most common and most talked of pathologic lesions, not only in gynecology but in surgery. It is replacing the surgery of the "cyst of the ovary." The author states that the disease is not such a frightening one as has previously been considered. The stage in which endometriosis is seen is often at the end of activity. Surgery for endometriosis should be done only for definite reasons, and significant symptoms are the real guides for such surgery. The excellent prognosis of this condition, the fact that in most cases the activity is over when it is recognized, means that unless definite symptoms such as sterility, severe dysmenorrhea and intestinal obstruction are present, endometriosis can be watched, just as well as patients with small fibroids.

The theory of the growth of the celomic epithelium due to delay in childbearing is the most important etiologic factor in endometriosis. The material studied in this paper consists of 2 series of 400 private patients and 2 series of 400 Massachusetts General Hospital patients. The first series of patients were collected in the years 1936-1941, and the second, 1945-1947. In the second private series 35 per cent of the cases operated upon abdominally for varied gynecologic complaints had endometriosis. The second series from Massachusetts General Hospital shows an 8.25 per cent involvement. It is evident that most patients with endometriosis are from the more well-to-do group. Also it is evident that late childbearing is the choice of private patients as compared to earlier marriage and many children among the ward patients. This investigation was carried out to prove that these impressions in the earlier series were not a misconception and that the same trend is evident in the latter series.

It being the writer's opinion that endometriosis occurs because of a lack of early and lack of frequent childbearing, he suggests how these factors affect the problem. Nature expects animals to mate early following the menarche and have offspring, nurse, and then become pregnant again, repeating this sequence until either physiologically they can have no more offspring or die. The human being does not carry out nature's rules. Late marriage and postponed pregnancy permits many menstrual cycles to occur and the varied hormonal reactions of menstruation probably stimulate the celomic cells to grow and produce müllerian growth. Menstruation is not supposed to occur monthly for years without interruption. The abnormal physiology of late and infrequent childbearing causes the growth of endometrial cells.

The author points out that the present economy of our country makes it almost impossible for a young man to support a wife, and he suggests that this behooves us as parents to help our children financially to marry early and have children. It is also suggested that higher wages be given to young married

The authors felt that in one of their cases the etiology of the endometriosis was repeated cauterizations and conizations of the cervix, plus a bad cervical laceration following a forceps delivery. They also felt that insufflations and injections of lipoid materials should be considered as etiologic factors. 2 figures.

(It is rather surprising that the authors were able to find only 11 reported cases of small bowel endometriosis, as I have personally observed 2 such instances, both marked and pseudoneoplastic, within the past few years. It is nothing like as common as is endometrial involvement of the rectum or sigmoid. It is of interest to note that endometriosis of the small bowel is not necessarily associated with pelvic endometriosis, and in 1 of my cases the pelvis was entirely free of aberrant endometrium.

I agree with the authors that even in older women in whom castration would not otherwise be objectionable, dependence on this alone is not safe with marked endometriosis of the small bowel, especially if symptoms of partial obstruction have already been present. The authors graphically describe the puckering and the fibrous tissue formation so often present, and this might persist even after castration, so that resection and anastomosis is the wiser plan.

Finally, the authors' belief that in one of their cases the etiology was "repeated cauterization and conization of the cervix, plus a bad cervical laceration following forceps delivery," seems to me a bit farfetched and implausible. By the same token, the etiologic role of tubal insufflation in endometriosis is a very doubtful one, to say the least. Our German colleagues used to charge us with producing endometriosis with our tubal insufflations, but Rubin and others have shown the complete lack of any incriminating evidence on this point.—Ed.)

AN EVALUATION OF THE TREATMENT OF ENDOMETRIOSIS

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Columbia, S. C.

South. Surg., 14: 645-650 (Sept.) 1948

The treatment of endometriosis is instituted primarily to relieve the patient of pain, abnormal bleeding, sterility, and occasionally intestinal obstruction or bladder symptoms. In order to do this, one has to keep in mind the age of the patient, the extent of involvement of the particular organ, the patient's marital status, and her desire for children. Certain measures should be taken prophylactically to prevent the development of endometriosis. Pelvic examinations, tubal insufflation tests, curettages or intrauterine manipulations are to be avoided at the time of menstruation. Anything which might obstruct the free flow of menstrual fluid along the usual channels should be corrected. The use of an impervious material to cover the abdominal incision during cesarean section might prevent the formation of endometriosis in the abdominal scar.

There are 3 major weapons available for active treatment of endometriosis: surgery, roentgen ray and testosterone, all of which may be needed at one time or another during the course of the disease. Each case requires close scrutiny before deciding on any course of therapy; however, a few generalizations can be

While many have found that endometriosis occurs much more often in private than in ward patients, and while this may possibly be due to the greater lack of early and frequent childbearing in the former, there is still need of supporting this view by statistical evidence as to the reproductive histories of patients in the various social groups. Just how such a factor would operate is not clear, and certainly I know of no scientific basis for Meigs' explanation that "the varied hormonal reactions of menstruation probably stimulate the celomic cells to grow and produce Müllerian growth." I do not think that the numerous adherents of the Sampson tubal regurgitation theory of the causation of endometriosis would accept such a theory.

While the author's advocacy of early and frequent childbearing is no doubt a sound one physiologically, for other reasons even more than that of endometriosis, it runs into the brick wall of economics. It is much too early and too Utopian to say that there "order be a law" that marriage must be entered upon by a certain age, and that contraception be legally banned. This would be planned economy with a vengeance, and many of us feel that the country has already been overdosed with this. I know that Dr. Meigs will not mind my little indulgence in this *reductio ad absurdum*. I agree with him that it "behoooves us as parents to help our children financially to marry early and have children," but large numbers of parents who have never heard of endometriosis practice and preach just the opposite. Whether right or wrong, therefore, there doesn't seem to be a great deal that can be done to apply the author's concept to the general control of endometriosis, and evangelistic work along this line will probably have to be by individual physicians to individual patients.—Ed.)

ENDOMETRIOSIS AS CAUSE OF SMALL BOWEL OBSTRUCTION: A REPORT OF THREE CASES

E. L. ZANDER, V. D'INGIANNI AND E. L. DREWES

New Orleans, Louisiana

J. Internat. Coll. Surg., 11: 149-153 (Mar.-Apr.) 1948

The writers have reviewed the English literature concerning endometriosis and have been able to find only 11 reported cases of this condition involving the small bowel. In 8 of these 11 cases there had been previous operations. Symptoms varied with the organs involved but the most constant complaints were dysmenorrhea, dyspareunia, sterility, intermenstrual pain, diarrhea and nausea and vomiting. Treatment was usually operative but bilateral oophorectomy alone has been suggested. However, it is doubtful if this by itself would relieve the obstruction because of the presence of a tremendous quantity of fibrous tissue which might eventually lead to cicatricial obstruction.

In the 3 cases reported in this paper, the site of involvement was close to the ileocecal area, varying from 6 cm. to 50 cm. from the ileocecal valve. A finding which was constant in these cases of intestinal obstruction due to endometriosis was the presence of a loop of ileum that was puckered or kinked, bound down by adhesions that were fibrous in type. Two of the patients reported made uneventful recoveries following resection and anastomosis but the third patient died of a massive pulmonary embolism after an apparently successful operation.

CLINICAL PATHOLOGICAL CONFERENCE: CHORIOEPITHELIOMA,
MIXED MESODERMAL TUMOR, AND LEIOMYOSARCOMA
OF THE UTERUS: THREE CASE REPORTS

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Minnesota Med., 31: 789-795 (July) 1948

The first case reported in this paper was that of a 31-year-old white female who was admitted to the hospital in the first trimester of pregnancy because of bleeding. Two other previous pregnancies had been uneventful. She was treated conservatively and the bleeding subsided. A second admission, with the same complaint, shortly after discharge was again handled conservatively, with cessation of bleeding. On the third admission the patient was bleeding and had cramp-like abdominal pains, and shortly after admission she passed two masses of placental tissue with grape-like cystic protrusions which microscopically were characteristic of a hydatidiform mole. One month later the Friedman test was positive and a total hysterectomy was performed. Pathologically, a friable tumor mass was found in the myometrium, and microscopic examination showed a typical chorioepithelioma. The patient is alive and well 2 years after her hysterectomy.

The writers review the literature concerning this type of tumor and find that it occurs relatively rarely. It occurs most commonly following the passage of a mole but has also been described as occurring after abortion or full term pregnancy. Bleeding is the most common early symptom, due to the invading anaplastic trophoblast elements. The diagnosis is facilitated by serial Friedman tests which will be positive many months before the tumor is clinically apparent. In certain cases radical surgery is indicated on the basis of this test alone, even in the presence of a normal-appearing uterus. The treatment is panhysterectomy; however, removal of the primary tumor does not appreciably affect the metastatic lesions.

The second case concerns a patient who was first seen at the age of 43 because of scanty menstruation and a "bearing-down" sensation. An enlarged, nodular uterus was found and the patient was treated with radium irradiation. She was seen periodically over the next 15 years and the size of the uterus decreased. She was again seen at the age of 59 with vaginal bleeding of 5 days' duration after 16 years of amenorrhea. The uterus at this time was found to be large, irregular and somewhat tender. There was a soft tumor mass extending from the opened external os. A supravaginal hysterectomy was done. Pathologically, the tumor was gray and soft and there were cystic areas. Microscopic examination revealed anaplastic smooth muscle, fibrous connective tissue, cartilage and striated muscle, as well as columnar epithelial lined glands. Necrosis, anaplasia, mitotic figures and tumor giant cells were noted. The diagnosis was mixed mesodermal tumor.

made. Some far advanced cases with "frozen" pelves should be treated with x-ray rather than attempting to remove all of the involved tissue surgically. It may be advisable that testosterone be used in small doses in the treatment of young women with endometriosis, in order to keep the disease in abeyance. The patient should be advised of her condition and of the problems with which she is faced in this connection. This is especially true in the case of young, single women who wish to be married and have children. There are times after palliative surgery when it is preferable to give a castrating dose of x-ray rather than subject the patient to another operation.

Of 65 patients in the author's series which have been followed over a prolonged period, 2 have had second operations, 2 have had enough pain to warrant x-ray castration and 3 have taken testosterone intermittently to control pain.

(I do not believe that I would include testosterone as one of the 3 major weapons in the treatment of endometriosis. Its effect is only temporary and palliative, as in the management of cases of residual endometriosis after operation. As a matter of fact, in most such cases in which there is sufficient menstrual pain to call for relief, I would prefer to depend on such simple analgesics as codeine and aspirin, especially as testosterone is likely to give very little relief unless it is begun a good many days before the usual onset of pain. When ectopic endometrium is left behind in the conservative treatment of endometriosis, it is usually a good plan to perform a presacral neurectomy at the same time, and this will usually prevent or greatly mitigate subsequent dysmenorrhea.

The author obviously is an ardent supporter of the Sampson theory of transtubal migration and peritoneal implantation of endometrium, since he warns of tubal insufflation at the time of menstruation, when I do not believe that anyone would do it anyhow, though chiefly on other grounds. The high incidence of endometriosis reported in almost all American clinics following the publication of Sampson's work in 1921 was explained by some European authors, notably in Germany, as due to the widespread practice of tubal insufflation in this country, though there is no practical support for such an idea.

In the treatment of the "frozen" pelvis seen in some cases of very advanced endometriosis I believe that surgery is generally to be preferred to x-ray, as it gives one the opportunity of determining the extent of the disease and the degree of involvement of the various pelvic organs, as well as the bladder and bowel. It is of course not necessary to remove all endometrial tissue in these extensive cases, nor would this always be possible. In these advanced cases, complete removal of the ovaries is the desideratum, any residual endometrial tissue undergoing retrogression. In some cases the local condition may make it impossible to remove all ovarian tissue, and in these subsequent x-ray therapy is often indicated.—Ed.)

which is certainly not true of the genuinely malignant chorioma. As a matter of fact, Ewing segregated this chorioadenoma destruens type chiefly to call attention to its favorable prognosis, while certain more recent authors stress it because of its supposed malignancy.

The chief characteristic of the genuine chorionepithelioma is the disorderly growth of trophoblast en masse, invading and destroying the uterine muscle, and commonly with no trace of a villous pattern. Ewing said he had never seen such a case get well, but a small proportion undoubtedly do. On the other hand, while I have had the opportunity of examining tissue from a rather large group, including considerable autopsy material, I do not believe I have ever seen a fatal case in which the histological picture was not that which I have mentioned above, nor have I seen a case of fatal metastasis in the so-called chorioadenoma destruens group. I may add that absence of villi has thus far been invariable in the uterine lesions of the fatal cases I have examined, although I can conceive that an occasional rare exception may be encountered in this regard.

All this discussion may not be at all pertinent to the case reported by the authors, and certainly is not to be construed as a reflection on the authenticity of their case report, which I am sure received competent pathological examination. I am moved to make these comments simply because my own experience has convinced me that proportionately more mistakes are made in this difficult field than in almost any other in pathology.

The second case reported by the authors is that of the rare mixed mesodermal tumor of the uterus, and the histological description leaves no doubt of the correctness of their diagnosis. Although the authors properly recommend panhysterectomy in such cases, I note that in their own case a supravaginal operation was done, but this may have been a matter of expediency dictated by existing conditions. The final case of this interesting group of tumors is one of uterine sarcoma, and this subject is sensibly and well discussed by the authors.—Ed.)

PROCIDENTIA COMPLICATED BY INTESTINAL STRANGULATION IN A POUCH OF DOUGLAS HERNIA

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J. Obst. & Gynaec. Brit. Emp., 55: 268-269 (June) 1948

The case is presented of a 50-year-old married woman who had had 2 normal deliveries and who had had the menopause one year prior to hospitalization. For about 7 years, her "womb had come right outside" but she had always been able to replace it herself. Forty-eight hours before admission she had vomited once and her "womb came down" but this time she was unable to correct it. Pain was present in the hypogastrium and the right iliac fossa and there was some difficulty of micturition.

Examination of the patient showed evidence of anemia. There was a persistent hiccough. The abdomen was distended. There was some vague tenderness in the hypogastrium. There was a large edematous procidentia which was replaced with some difficulty and which recurred immediately after pressure was released. It was held *in situ* by a cup and stem pessary. The blood urea was

The histogenesis of these tumors is uncertain but it has been suggested that they arise from embryonic rests. They are more frequent after the menopause and are seen most commonly in the body of the uterus. The symptoms of these tumors are bleeding, discharge and pressure symptoms. Local recurrences are common and distant metastases are seen. They are malignant out of proportion to their histology, with a mortality rate of 95 per cent. Treatment consists of panhysterectomy followed by irradiation. However, no 5-year cures have been reported.

The third patient was a 58-year-old woman who complained of swelling of her abdomen, a sensation of weight in the pelvis and 20 pounds' weight loss of 3 months' duration. On examination, the tumor mass was found to fill the entire pelvis and on laparotomy it was found to lie retroperitoneally. Part of the tumor had to be resected close to the abdomen. The patient went into shock and died shortly after the operation.

On cut section the tumor nodules were made up primarily of firm grayish tissue with many areas of degeneration and necrosis. Microscopically, there was a highly anaplastic cellular growth with elongated nuclei and scanty cytoplasm. Mitotic figures and tumor giant cells were noted. A diagnosis of leiomyosarcoma was made.

This tumor which usually arises from the myometrium may be primary or may occur in a pre-existing leiomyoma, the latter being the most common finding. It is thought that about 0.5 to 1.5 per cent of the benign tumors become sarcomatous. They are found most frequently at the menopause. The following findings at the time of operation suggest the presence of a sarcoma in a leiomyoma: (1) unusual friability of the broad ligament; (2) unusual vascularity of the tumor; (3) absence of a sharp line of demarcation between the tumor and myometrium; (4) the opaque pork or brain-like appearance instead of the usual glistening whorl-like appearance. The symptoms of these tumors are not distinctive and resemble those of ordinary leiomyomata until late in the disease. The 5-year salvage, as reported in the literature, averages around 30 per cent and depends, to an extent, on whether the tumor is primary or secondary, and on the age of the patient. The degree of malignancy seems to be directly related to the mitotic count of the original tumor. The accepted treatment is panhysterectomy and deep x-ray therapy. 6 figures.

(It may seem to be an unjustifiably lofty attitude to take, but I confess I am always extremely skeptical of reports of cures of chorionepithelioma, especially those following hydatidiform mole, unless representative sections or good photomicrographs are available. The reason for this is that such a diagnosis is often made in cases of hydatidiform mole associated with marked trophoblastic overgrowth, with or without pronounced penetration of the vascular channels. Moles of this type are often spoken of as chorioadenoma destruens or malignant mole, but histologically the trophoblast is often, except for its quantity, not demonstrably different from that of moles which are cured by simple evacuation. It is true that the chorioadenoma destruens, an ill-advised but now popular term coined by the late James Ewing, may in some cases lead to fatal bleeding, either vaginal or abdominal. But the villous pattern is always well-preserved and such lesions do not metastasize, as does a genuine chorionepithelioma. Further, they are always curable by hysterectomy,

Areas of diffuse cellular growth appear in grade 3. Cellular growth is diffuse and lacking in any glandular pattern in grade 4.

Morphology of the tumor did not remain static; in 13 of the 18 rabbits the tumor progressed from grade 2 to grade 4 at autopsy. Gradual transitional changes were noted in consecutive biopsy specimens. Five of the tumors remained static and metastases occurred in only 2 cases. Six of the animals were free of metastases at death. In half the cases the metastases and the tumor were at the same grade at autopsy.

The incidence of takes and the growth rates of the homologous transfers form a biological index of the developmental state of the tumor. Both incidences increased with the age of the tumor. Some significant developments were not attended by commensurate histological alterations. Development of the tumor either morphologically or biologically depended on residence in the host. Transferred tumors persisted but did not advance, nor was the incidence of takes and the growth rate changed. Therefore, development into cancer appeared dependent on factors in the spontaneous host.

Autologous transfers were made at the laparotomy incision and in the anterior chamber of the eye. The activity was more pronounced in the subcutaneous tissue than in the eye chamber.

Irregular distribution of factors concerned in tumor development is illustrated in Case 15. At death tumor tissue of all grades was present in the one animal.

The authors feel that cancer is the final stage in the developmental process beginning in a neoplastic focus and dependent on factors peculiar to the host and not found in normal animals. These factors aid progression to the malignant and metastatic state. 24 figures.

(Two lessons of practical value would seem to emerge from this interesting study. One would pertain to the histological gradation of tumors, since the authors find that changes in gradation occurred in the course of transplanted cancers in 13 of 18 rabbits, and incidentally in an advance from Grade 2 to Grade 4. The fact that consecutive biopsies showed a gradual transition in this respect is of interest, and perhaps can be applied to similar evaluation of histological gradation in the human. Another point touched upon more lightly in the paper is the role of organ environment in metastatic tumors, a question which deserves much more study than it has received. The pattern of the primary growth may undergo considerable change when the tumor is planted by metastasis in another organ. A striking example of this is seen in the well-known Krukenberg tumor of the ovary, the microscopic picture of which is far different from that of the gastrointestinal primary growth.—Ed.)

153 mgm. per cent. The leukocyte count was 15,900 with 81 per cent polymorphonuclears.

The patient continued to vomit and the pulse remained elevated. An x-ray of the abdomen confirmed the diagnosis of a small bowel obstruction, so a laparotomy was performed. The gut was found to be distended and the coils of small intestine were followed down to a constricted ring behind the uterus which was the entrance to the pouch of Douglas. The ring was large enough to admit one finger. The gut was delivered and a gangrenous segment about one inch in length was found. This was resected and an end-to-end anastomosis was performed. Postoperatively the patient did poorly, gradually becoming more comatose and dying on the second postoperative day.

This condition is apparently quite rare, and a review of the literature by the author revealed no similar cases. The diagnosis could probably best be made on the basis of the history of procidentia of many years' duration plus the concomitant signs of small bowel obstruction.

(This is certainly a rare type of obstruction, and, indeed, the author has been able to find no similar case in the literature. This seems rather strange, since vaginal hernias are not extremely rare, and sometimes the neck of the hernial sac is comparatively small even when the sac contains a considerable amount of intestine. One wonders why the possibilities of strangulation are not about as great as with a scrotal hernia in the male.—Ed.)

EVOLUTION OF CANCER OF THE UTERINE FUNDUS IN THE RABBIT

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Cancer, 1: 82-99 (May) 1948

The continued investigation of adenocarcinoma of the uterine fundus in the rabbit is reported. The object of the experiment was to study and compare the transplantability and growth rate of the cancers at different phases of development. Laparotomies were performed at various intervals and fragments removed. Portions of the fragments were fixed for histologic study and homologous and autologous transplants were made with the remainder.

Homologous transfers were made to normal, unrelated animals of the same species to determine the progress of developmental changes in the tumor itself, independent of features in the primary host.

Autologous transfer was carried out to determine the behavior of the tumor at different sites in the host. Laparotomies and autopsies are outlined in Table 1 of the paper.

A system of grading based on morphological development was possible. Grade 1 consisted of a simple reduplication of endometrial glands separated by abundant stroma. In grade 2, either acinous or papillary architecture is found.

The above comments do not of course apply to those cases in which the pelvic tuberculosis is only a part, and sometimes a subordinate part, of an extensive peritoneal tuberculosis, or in which there is a very active pulmonary lesion. In this group operation is to be avoided, and dependence put on prolonged rest and other appropriate means of combatting the tuberculous process, especially when it involves the lungs. It is in cases of this sort that abdominal x-ray therapy has been employed with advantage. This plan has been widely employed in the South American clinics for many years, not only in cases of the type above described, but also in those in which the disease has apparently been limited to the pelvic organs. Unfortunately, in most of this group the diagnosis is not made until after operation, and usually not until after microscopic examination. The results obtained by Campbell in the treatment of experimentally produced pelvic tuberculosis in rabbits suggest that x-ray therapy may be a valuable addition to our armamentarium in at least some cases of genital tuberculosis (See Survey comment on abstract of paper by Ralph Campbell on "The treatment of pelvic tuberculosis in the female by radiation therapy based upon experimental evidence in the animal and clinical results in the human, *Obst. & Gynec. Surv.* 2: 575, 1947.—Ed.)

A CASE OF ADENOMYOSIS OF THE UTERUS
WITH TUBERCULOUS INFECTION

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J. Obst. & Gynaec. Brit. Emp., 55: 180-183 (April) 1948

A case of adenomyosis uteri with tuberculous infection is described and a plea is made for radical operative treatment in tuberculosis of the uterus and adnexa.

The patient was aged 38 years and was admitted as an emergency with uterine hemorrhage. There was a history of severe uterine hemorrhage of 14 days' duration and occasional attacks of lower abdominal pain. She had been curetted 4 times and in one a microscopic diagnosis of tuberculous endometritis had been made. Chest x-ray was negative. A large mass filled the lower abdomen and extended to the umbilicus. Following blood transfusions a diagnostic curettage was done; the microscopic findings confirmed the previous report of tuberculosis.

Operation was performed 4 days after admission. The small intestine, transverse colon and pelvic colon were densely adherent to the uterine mass. These were dissected off and the uterus was shelled out and removed with the cervix. The vagina was loosely sutured. Penicillin, which had been given preoperatively, was continued for 10 days after operation. Six days after operation the abdominal wound opened down to the bowel. Secondary suture was carried out, with subsequent excellent union. Seven months later the pelvis appeared completely clear, there was no vaginal shortening, the abdominal wound had healed well and the patient's general condition was excellent.

Sections of the uterine wall and tumor showed the tumor to be of typical adenomyomatous structure. In some areas grouped around the glandular elements were numerous giant-celled masses typical of a tuberculous infection, obviously a very heavy one. 4 figures.

(The association of adenomyosis with tuberculosis of the tubes and later of the uterus is uncommon, though there appears to be no reason why the 2 conditions should not occasionally coexist. In this case the tuberculosis was apparently quite extensive, and the dense intestinal adhesions which are described imposed some hazard of postoperative fistula, though this did not occur. The removal of the uterus as well as the adnexa in cases of this extent would certainly be endorsed by most gynecologists, even though the previous curettage had not revealed definite evidence of uterine tuberculosis. The latter can be almost assumed in cases of very longstanding tubal tuberculosis.

There are some gynecologists who, in the case of younger women with tubal tuberculosis, conserve the uterus and menstrual function with the feeling that once the primary tubal focus has been removed, a proper constitutional regime will enable the uterus to throw off a tuberculous infection if this has already occurred. I believe that the majority, however, will believe that, since removal of the tubes prevents later pregnancy anyhow, it is safer also to remove the uterus rather than to trust to the *vis medicatrix naturae* when dealing with a disease as serious as tuberculosis. The ovaries can safely be conserved in almost all cases, since they usually show no involvement, though there are some exceptions. For example, I have seen even large tuberculous abscesses in association with comparatively mild tubal tuberculosis.

Pictures of the 6 malignancies are included and discussed by the author. 10 figures.

(This complete and authoritative discussion of primary tubal carcinoma emphasizes the insidiousness of this rare neoplasm. It is very infrequently diagnosed preoperatively, and then on a presumptive basis only. The presence of a unilateral adnexal mass of moderate size, associated with postmenopausal staining or scant bleeding, should lead one to include tubal cancer among the diagnostic possibilities, but the rarity of the tumor is far more likely to suggest other much more common lesions, especially ovarian carcinoma. In many cases the very size and ovarian contour of the mass justify the feeling that the ovary and not the tube is the seat of the tumor.)

Emge points out that the vaginal smear may be of occasional value in the diagnosis of tubal cancer, and this, as a matter of fact, has already been demonstrated in one or two reported cases. If, for example, malignant cells are revealed in the smear, and thorough biopsy studies of the cervix and endometrial scrapings show no trace of cancer, one would be justified in turning one's suspicion to the tube, especially if there is any palpatory suggestion of tubal enlargement. Even under these conditions one could not altogether exclude the possibility of early ovarian cancer, some of the cells of which may occasionally find their way into the genital canal. But in any event, early operation in such cases will greatly enhance the possibility of cure, whether the cancer is tubal or ovarian in origin. There is reason to feel that the rarity of cure from tubal cancer is not to be altogether explained by any intrinsic degree of malignancy but is largely due to the fact that the disease has commonly reached an advanced stage before recognition and operation. As a matter of fact, the occasional early case is practically always a lucky accidental find. The most striking instance of this sort that I know of is the one reported by Mitchell and Moehler (*Am. J. Obst. & Gynec.* 50: 283, 1945). In this case the routine microscopic examination of the small loops of tube excised at a tubal sterilization operation showed in one loop a very early carcinoma. Through the kindness of Dr. Moehler I had the opportunity of studying sections of this lesion, and there is no doubt that it represents a typical primary tubal carcinoma of the characteristic papillary pattern. This patient, I believe, is still entirely well.—Ed.)

FIBROMYOMA OF THE FALLOPIAN TUBE

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Royal Northern Infirmary, Inverness

J. Obst. & Gynaec. Brit. Emp., 55: 155-158 (April) 1948

The Fallopian tube is a rare site of tumor formation, and Dietrich (1922) states that among the rarest of all such neoplasms is the fibromyoma. The diagnosis of this type of tumor is extremely difficult and is said never to have been made preoperatively. The symptomatology is not characteristic.

The author reports the case of a 45-year-old woman who had had one pregnancy 25 years ago, followed by sterility. There had been frequency of micturition for about one year. Following sea-bathing 7 days prior to admission, she suffered from lower abdominal pain, vomiting and diarrhea, followed by persistent suprapubic pain. A solid tumor could be felt arising from the pelvis that

THE ADNEXA

SIX CASES OF PRIMARY CARCINOMA OF THE FALLOPIAN TUBE

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West. J. Surg., 56: 334-345 (June) 1948

Six cases of primary carcinoma of the Fallopian tube are presented. These cases represent an incidence of .44 per cent of the genital cancers listed in the Stanford University, Department of Gynecology, files.

This relatively rare cancer is not only insidious in its growth habits but most confusing in its symptomatic manifestations. Of the 6 cases reported in this paper 2 were diagnosed preoperatively as ovarian malignancy, one as ovarian cyst, one as giant hydrosalpinx and one as endometriosis with menopausal bleeding. However, the writer holds that it is not so great an omission to fail to diagnose this symptomatically obscure disease as it is to fail to recognize the need for pelvic exploration whenever an obscure pelvic condition develops in the cancer age groups. Furthermore, he feels that radical surgery with a possible chance of cure is justified.

Symptomatic manifestations of tubal cancer are almost indistinguishable from pelvic inflammatory disease. Fever, leukocytosis, and an increase in sedimentation rate with inflammations overshadow the true nature of the disease. Uterine discharge is not as common a symptom as is sometimes thought. Only one of the cases discussed here had a purulent discharge which, at the age of 34 and in the presence of pelvic inflammation, did not suggest malignancy. Three patients complained of uterine bleeding but had no pain in spite of sizable adnexal tumors. It is not unusual for large but localized tubal malignancies to remain asymptomatic for a considerable period of time.

Further development and wider use of the vaginal smear method will be of value in the early recognition of tubal cancer. The use of hysterosalpingography seems to be neither safe nor practical. If the tube is closed it is impossible, and if the tube is patent, and forceful entrance is made, dissemination of the neoplasm may occur. Highly important is the recognition that the triad of lower abdominal pain, watery or bloody discharge and lateral pelvic mass connotes the possibility of tubal cancer and calls for prompt surgical exploration. Inflammatory manifestations, at the age when pelvic inflammations are uncommon, are also suggestive of the disease.

Treatment of primary tubal carcinoma is surgical and should be as radical as possible. Invasion of the neighboring viscera indicates palliation through roentgenotherapy; however, tubal cancer seems highly resistant to irradiation. None of the 6 patients lived longer than 20 months after the recognition of the disease. A salvage rate of 3 per cent is perhaps optimistic.

Pictures of the 6 malignancies are included and discussed by the author. 10 figures.

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was firm and of limited mobility; it was slightly tender and appeared to be a uterine fibroid. Immediate laparotomy revealed that the mass in the abdomen consisted of edematous omentum wrapped around a tumor arising from the left uterine appendage. The omentum was separated and the tumor identified as a pedunculated fibroid arising from the middle third of the tube which had undergone torsion through $1\frac{1}{2}$ complete turns. The torsion was undone and the tumor, together with the corresponding tube, was removed. There were no uterine fibroids or other evidence of pelvic disease. Two months later the patient was symptom-free. 1 figure.

HYDATIDIFORM MOLE IN THE FALLOPIAN TUBE

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J. Obst. & Gynaec. Brit. Emp., 55: 322-324 (June) 1948

The author has reviewed the literature relating to hydatidiform mole of the Fallopian tube and has found the condition to be extremely rare. Only 14 acceptable cases have previously been reported. On the other hand, chorionepithelioma, usually an uncommon sequela of a mole, has been reported as developing in the Fallopian tube 3 times as frequently as a hydatidiform mole. The Aschheim-Zondek reaction is not of value in distinguishing between tubal pregnancy with a normal ovum, and that with a hydatidiform mole. The treatment is that of any tubal pregnancy but careful follow-up with biological tests is demanded to exclude subsequent malignant degeneration. The prognosis is good and better relatively than in uterine hydatidiform mole where the uterus is ordinarily left in situ.

A case is reported of a married woman, aged 35 years, who gave a history typical of ectopic pregnancy with amenorrhea, irregular bleeding and lower abdominal pain. No adnexal tumor could be palpated. A laparotomy was performed and a small amount of blood was found in the pelvis. The left tube was normal but the right tube contained a small swelling in its mid portion, measuring 1 cm. by 2.5 cm., and there was a minute rupture over this swelling. The right tube was removed and the patient made an uneventful recovery. Since operation, the Aschheim-Zondek test has been negative. On section of the tumor a yellowish-red hematoma was found with a cyst-like cavity enclosed in it; no embryo was found. Microscopically, typical decidua and abnormal chorionic villi were present, many of the villi having undergone degeneration and swelling of the hydatidiform type.

(Hydatidiform mole in the tube is, as the author states, a rare finding, although there would seem to be no reason why it could not develop here as readily as in the uterus. Perhaps this statement should be qualified, as we do not as yet know the etiology of this con-

dition. As a matter of fact, certain investigators, like Arthur W. Meyer (*Am. J. Obst. & Dis. Women* 78: 1, 1918), believe tubal hydatidiform mole, as well as the far more common uterine variety, is extremely frequent, since they accept as the only necessary criterion of this condition the absence or extreme scantiness of stromal blood vessels, even though there is little hydrops and none of the trophoblastic proliferation which others include in the criteria. These authors believe that the simple changes which they describe represent very early stages of the lesion which in its fully developed vesicular form we designate as hydatidiform mole.

Exactly the same view had been expressed by Gierse as far back as 1847, and was revived by Storch in 1878. However, it has never won acceptance, chiefly because no one has established satisfactory transition stages between the supposedly early stages described by these observers and the full blown hydatidiform mole. It seems probable that the avascular and perhaps slightly cystic villi described by Meyer represent degenerative phases of the chorionic villi. They lack the trophoblastic proliferation which in some cases is very pronounced, and which, in my experience, is always to be found if the villi are examined *in situ*, still attached to the uterine wall. One is apt to get a wrong impression if, as is so often the case, only evacuated or curetted material is examined. The grape-like vesicles which so often fill the uterine cavity are ordinarily degenerated because they have grown away from their blood supply. They therefore often show little or no trophoblastic overgrowth.—Ed.)

UNILATERAL HYDROSALPINX WITH TORSION WITHOUT INVOLVEMENT OF THE OVARY: CASE REPORT

R. H. KAZMIERSKI

Condersport, Pa.

Pennsylvania M. J., 51: 1416-1417, (Sept.) 1948

The patient whose case is reported in this paper was a 14-year-old girl who was admitted to the hospital with the complaints of right lower quadrant pain, nausea and vomiting of 24 hours' duration. The menstrual history was normal and the past history was non-contributory except for a similar attack one year previously. The white blood count was 13,300 with 72 per cent polymorphonuclears and 28 per cent lymphocytes. The preoperative diagnosis was acute appendicitis.

At operation, 800 cc. of serosanguinous fluid was found in the abdominal cavity. The right ovary was cystic and the uterus was anteverted with somewhat taut ligaments. The right tube was twisted on its pedicle 3 turns counterclockwise, and the distal third was jet black. Microscopic section revealed recent hemorrhage. The patient had an uneventful recovery.

A review of the literature reveals that this is a relatively rare condition that occurs more frequently on the right side. The present case is the eighth such case reported since 1942. The author points out that it can easily be mistaken for other acute abdominal conditions. He feels that in this case the anteversion of the uterus and the congestion developing at the time of ovulation were responsible for the precipitation of torsion and subsequent hydrosalpinx.

(While the occurrence is not common, there have been a good many cases reported of torsion of a hydrosalpinx, with or without the adjacent ovary. For that matter, even a normal tube, or a tube and ovary, may be involved in such torsion. This is of interest and importance in the interpretation of those rare cases in which at operation in patients who have had no previous laparotomy, the surgeon is surprised to find what is apparently a complete congenital absence of one tube and ovary. On closer examination, however, a short stump of the tube is seen, much like the stump of an amputated tube. The explanation is that at some previous time, perhaps many years before and possibly even in very early life, the tube and ovary have twisted themselves off, with later complete resorption. I have encountered 3 cases of this type. As a matter of fact even rather large ovarian tumors have been reported to have thus undergone torsion and resorption.—Ed.)

PRIMARY TERATOMATOUS CHORIONEPITHELIOMA OF THE OVARY: REPORT OF A CASE

H. M. OLIVER AND E. O. HORNE

Worcester City Hospital, Worcester, Mass.

New England J. Med., 239: 14-16, July 1, 1948

Chorionepithelioma may arise from uterine or ectopic pregnancy or a teratoma. A case of the latter is added to the 13 cases found in the literature.

A primary ovarian chorionepithelioma can be assumed only in a child. Symptoms of the reported cases have included precocious sexual development, vaginal bleeding, abdominal swelling or pain. Some cases have had no typical symptoms. Clinical diagnosis can be made by a positive pregnancy test with dilute urine or spinal fluid. Treatment is unsatisfactory and survival after removal of the uterus and ovaries is 8 months.

An 11-year-old girl was seen in the accident ward, complaining of low abdominal pain. She improved after 24 hours and was discharged. Six weeks later she returned with constant dull hypogastric pain. No other symptoms were present and the patient had never menstruated. Palpation of the abdomen revealed a lemon-sized mass in the lower right quadrant which extended 5 cm. above the symphysis to the right of the midline. It was freely movable and nontender. No muscle spasm or fluid wave was present. In view of the previous attack it was believed that the patient had appendicitis with rupture and abscess formation, although the white cell count was only 6400 with 61 per cent neutrophils, and the sedimentation rate was 35 mm. in 1 hour.

Laparotomy revealed a normal appendix. But a large hemorrhagic, necrotic tumor of the right ovary was clearly visualized. The entire mass, including the tube, was excised. There was no evidence of metastasis; the uterus, left ovary and tube appeared normal.

The immediate postoperative course was uneventful. On the third day the patient began to menstruate, the hemoglobin fell to 49 per cent and transfusions were given. A Friedman test, at first negative, was positive 10 days later. Twenty-one X-ray treatments were given.

The patient was discharged on the 65th day. The Friedman test remained positive despite radiation therapy. She lost weight and could not return to the clinic for examinations. The family physician stated that a large nontender mass developed in the abdomen. The patient died 4 months after operation. Autopsy permission was not granted.

Upon examination the ovarian mass measured 7.5 by 7 by 7 cm. with a smooth mottled blue and red sheen. There were numerous cysts with a smooth lining of stratified epithelium. The greater part of the cortex and medulla was hemorrhagic and necrotic. Several masses of round to cuboidal cells representing Langhans cells were found. Syncytical cells were found in the walls between the masses. 2 figures.

(Primary chorionepithelioma of the ovary, as the authors state, is exceedingly rare, much more so than the corresponding tumor in the male gonad. A large number of testicular teratomas containing chorionepitheliomatous elements, have been reported, and yet, in the ovary, which is not infrequently the seat of teratoma, chorionepithelioma has been found in only a small group of cases. One would hardly expect to find chorionepithelioma with the simplest type of ovarian teratoma, the dermoid cyst, since the alien tissues present in the latter are usually of mature type, and dominantly ectodermal. But in the far less common malignant teratomas the motley conglomeration of alien tissue elements is often of immature and even embryonic type, so that it is not surprising that malignant chorionic tumors may develop.—Ed.)

VIRILIZING TUMOURS OF THE OVARY; WITH REPORT OF A CASE ASSOCIATED WITH PREGNANCY

W. N. SEARLE, M. HAINES AND J. K. BAKER

Chelsea Hospital for Women

J. Obst. & Gynaec. Brit. Emp., 55: 135-141 (April) 1948

The authors report a case of adrenal-like ovarian tumor associated with pregnancy. The patient, aged 33 years, was seen when estimated to be about 34 weeks pregnant. Her pregnancy had proceeded normally until about the 24th week, when she had noticed a great increase in growth of hair on the face and deepening of the voice. There had been no perception of fetal movements.

Examination revealed a growth of coarse black hair on the chin extending upward in normal male distribution to the hair line on the scalp. The pubic hair showed a male distribution with a certain amount of hirsutism between the umbilicus and ensiform cartilage. The voice was deep and masculine. Psychologically, the patient seemed normal. Her sexual interest, which had always been mild, had not been affected either by the pregnancy or by the development of symptoms. The blood pressure was 170/120. The uterine fundus corresponded to a 27 weeks' gestation and the fetus presented by vertex. Hypertrophy of the clitoris was present. Fetal movements were felt and the fetal heart clearly heard. No pelvic tumor was palpable.

One month later the patient went into labor, and after 3 hours a living male child was born. The infant weighed 5 pounds, 6 ounces and showed no gross evidence of prematurity. The puerperium was normal except that lactation was not established.

One month after delivery a laparotomy was carried out. The suprarenals were palpated and nothing abnormal detected. However, a cystic mass about the size of a cricket ball was found lying anteriorly to the right broad ligament. The cyst was excised and its long pedicle buried.

Following operation, the loss of abnormal hair did not begin for 3 months, but then went steadily to complete restoration of the female distribution in 6 weeks. The voice has not recovered after nearly 5 years. Neither the macroscopic appearance of the tumor nor the subsequent history of the patient suggests malignancy.

Urinary hormone excretion is shown in relation to clinical events in the following table:

<i>Date</i>	<i>Patient's urine</i>
Dec. 30, 1942	158 mg. ketosteroids per day.
Jan. 11, 1943	Infant born.
Feb. 2, 1943	23 mg. ketosteroids per day.
Feb. 10, 1943	Ovarian cyst removed.
Feb. 15, 1943	12.8 mg. ketosteroids per day.
Feb. 12, 1943	Infant's urine: 13.8 mg. ketosteroids <i>per liter</i> .

Histologically, the tumor was composed of a loose connective tissue groundwork in which were set irregular sheets or masses of polyhedral cells. Blood vessels were frequent. There were several small areas of lymphocytes. The tumor cells resembled those of the adrenal cortex. The cytoplasm stained in a variety of ways, the general rule being for a semi-clear or granular appearance. In others the cytoplasm was more diffuse but pale pink. Other cells showed distinct brownish granules. Lastly, there were cells occurring singly or in clusters in which the cytoplasm stained heavily and was bright pink. The nuclei showed great variation in size; where the nucleus was unusually large it was often hyperchromatic as well. Distinct nucleoli were present. Mitoses were scarce.

Two possibilities as to derivation of this tumor are discussed. First, the tumor may be derived from the corpus luteum. From the cytological picture there is not enough evidence to call this a tumor, in the sense of neoplasia. There were patches of marginal theca cells, pointing to a corpus luteum origin. But it is difficult, in the present state of our knowledge, to appreciate how this pre-eminently feminine structure would secrete androgens. It seems apparent that this tissue did secrete androgens, for their output fell after its removal. Adrenal rest tissue would be capable of androgen production but the stimulus seems to have come from outside the ovary and, therefore, outside the adrenal-like tissue. Androgen excretion fell appreciably after birth and before the ovary was removed. This latter fact indicates that the gestation was in some way, either through the placenta or the hypophysis, responsible for the stimulus.

The corpus luteum in early pregnancy elaborates progesterone and after the

third month generally ceases to be functional. It is suggested that in this case it took on an abnormal function, namely the elaboration of androgens. 3 figures.

(From the description given of the histology of this tumor one gets the impression that it belongs to the group variously designated as adrenal cell tumor, virilizing lipoid cell or hypernephroid tumor, masculinovoblastoma or luteoma. The authors themselves express doubt that a preeminently feminine structure like the corpus luteum could secrete androgens, and yet in the last paragraph they suggest that in this case the corpus luteum of pregnancy took on the abnormal function of elaborating androgens. This does not sound very plausible, although no one knows enough concerning the histogenesis and the biological potentialities of lesions of this general type to justify any arbitrariness of view-point.

My own feeling is that the term luteoma should for the present be limited only to the definitely feminizing tumors in which virtually complete luteinization of granulosa cell tumors has occurred. I agree with Schiller that the masculinizing "luteomas" do not arise from lutein cells. Whether they are of adrenal type is another question. In some cases they probably are. However, there are some, like Teilum, who look upon these tumors as representing a neoplastic overgrowth of the cells of Leydig, which normally, like all other elements of both the female and the male gonads, are ultimately derived from the gonadal mesenchyme, according to the prevailing embryological opinion of the present day. Still others, like Iverson, are inclined to the belief that the source is to be sought in the theca interna cells. I have discussed these various viewpoints more fully in a paper just published in the December number of the Journal of Obstetrics and Gynecology of the British Empire.

Incidentally, it is interesting that the occurrence of such masculinizing tumors as arrhenoblastoma, as well as the feminizing granulosa cell tumors and the hormonally inert dysgerminomas, is not, on the basis of a number of reported cases, incompatible with the occurrence and normal progress of pregnancy, and that such tumors have not appeared to exert any harmful effect upon the fetus. The case reported in this abstract is the first one, so far as I know, in which a tumor of the so-called adrenal type has been noted during pregnancy.—Ed.)

THECA CELL TUMORS OF THE OVARY WITH A REPORT OF FIFTEEN CASES AND A REVIEW OF THE LITERATURE

W. R. KNIGHT, III

Houston, Texas

University of Wisconsin, Madison, Wis.

Am. J. Obst. & Gynec., 56: 311-324, 1948

The author has presented a clinical and pathological review of 15 cases of theca-cell tumor, in one of which the tumor weighed 7,727 gm. Biological assay of this tumor revealed the equivalent of 0.2 gamma of estrone per 100 grams of extracted tissue and there was no appreciable amount of progesterone present. Although the estrogen produced by thecomas is small, its effect is prolonged and unopposed by the action of progesterone, which may account for the symptoms and frequent occurrence of associated pathology, such as menstrual irregularities, postmeno-

pausal bleeding, endometrial hyperplasia, adenomyosis, hypertrophy of the myometrium with uterine enlargement, uterine myomas and endometrial carcinoma.

In this series the thecoma occurred most frequently in the fifth and sixth decades and 61.5 per cent of the patients were past 50 years of age. The most characteristic feature of this tumor was the distinctive diffuse yellow color seen on cut section, and this was present in 100 per cent of the cases. Uterine curettage should be done in all cases to rule out associated adenocarcinoma of the endometrium.

The author feels that conservative surgery is indicated in the premenopausal patient. However, if the thecoma is associated with adenocarcinoma of the endometrium, total hysterectomy is always the operation of choice. 4 figures.

(It is difficult to correlate the clinical symptoms of thecoma, and the same applies to granulosa cell tumors, with the size of the tumor or with the estrogen production of the growth as determined by biological assay. I recall one case of thecoma in which rather free, menstruation-like postmenopausal bleeding had occurred for a good many months, although the growth was scarcely more than 1 cm. in diameter. The yellowish hue of these tumors, as well as parts of granulosa cell tumors and arrhenoblastomas, is quite characteristic, and is evidently due to the rather rich lipid content of these growths. The author's recommendation of conservative surgery for such tumors in the younger group of patients will be generally endorsed.—Ed.)

PSEUDOMUCINOUS CYSTADENOCARCINOMA OF THE LEFT OVARY

G. C. CAUSEY AND J. C. McCARTER

Northwestern University Hospital, Chicago, Ill.

Quart. Bull. Northwestern Univ. Med. School, 22: 232-235 (Fall) 1948

A case is presented of a 34 year old woman admitted to the hospital complaining of a dry cough, fatigue, dull pain in the upper abdomen and lower left chest, hemoptysis, marked dyspnea and low grade fever. Physical examination revealed dullness and a few rales in the left lung base. A firm, irregular mass was palpated in the lower abdomen. The uterus was of normal size. The history of the menses was regular.

Chest X-rays showed a rapid advance in the lesions. Differential diagnosis was between virus pneumonia with carcinomatosis and carcinomatosis with a probable primary site in the left ovary, and lung metastases.

The patient died before the diagnosis could be established. Pathological findings revealed pseudomucinous cystadenocarcinoma of the left ovary with widespread metastases to the uterus, adnexa, peritoneum, stomach, and both lungs.

(It is easy to understand that the diagnostic problem in this case was made difficult by the poor condition of the patient, which probably made impossible the bronchoscopic ex-

examinations which are often of value in the diagnosis of pulmonary cancer. It would seem that in a case of the type described examination of the sputum for cancer cells might have been of value.—Ed.)

UNRUPTURED PRIMARY OVARIAN PREGNANCY

S. S. WITTENBERG AND R. G. RIES

Detroit, Michigan

Ann. J. Surg., 75: 618-623, 1948

A review of the reported cases of primary ovarian pregnancy is presented with the observation that such cases are still a rarity. A new case is presented of a 23-year-old patient who complained of pain in the lower right quadrant, irregular menstrual bleeding, dyspareunia and dyschezia. Moderate vaginal bleeding and pain and fullness of the breasts had been present for several weeks. The general physical examination was essentially negative. Pelvic examination revealed a slightly tender, doughy mass about the size of an egg in the right adnexal region. The clinical impression was that of chronic pelvic inflammatory disease, and the patient was put to bed and given sulfadiazine. Several days later vaginal bleeding was still present and the right adnexal mass was the size of an orange. The tentative diagnosis was a corpus luteum cyst. Operation revealed no blood in the peritoneal cavity but the right ovary, except for one pole, was replaced by a hemorrhagic, discrete, doughy, cystic mass with adhesions to the uterine and broad ligaments. The right tube was completely normal. A right oöphorectomy was performed and the postoperative course was uneventful.

The pathologist reported an ovary with a centrally located cyst lined with a sac-like membrane. There was no rupture of the sac at any point and no fetus was found. Microscopically, ovarian tissue was found. The sac membrane consisted of amnion and chorion surrounded by a layer of blood clot containing chorionic villi. The diagnosis was unruptured ovarian pregnancy.

In this case, Spiegelberg's criteria are fulfilled; namely, (1) the fallopian tube on the affected side was intact and separate; (2) the gestation sac occupied the position of the ovary; (3) the sac was connected with the uterus by the broad ligament; and (4) ovarian tissue was found in the sac wall. Classification of primary ovarian pregnancy was made on the basis of the total absence of any foreign tissue other than the gestation elements.

A discussion of the mechanism of ovarian pregnancy is given and the authors discuss four methods of ovarian implantation: intrafollicular, interstitial or parafollicular, superficial and superfollicular implantation. Ovarian implantation is pathologic, since the ovary is unfit for this purpose; the usual course is an early rupture of the ovary within the first trimester. However, the ovum may die and be absorbed or degenerate and form a tumor. A higher percentage of

pausal bleeding, endometrial hyperplasia, adenomyosis, hypertrophy of the myometrium with uterine enlargement, uterine myomas and endometrial carcinoma.

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FEMALE UROLOGY

THE REPAIR OF VESICO-VAGINAL FISTULA FOLLOWING RADIUM TREATMENT FOR CARCINOMA OF THE CERVIX

S. RUSSELL

Manchester, England

J. Obst. & Gynaec. Brit Emp., 55: 334 (June) 1948

The author has established certain principles to be followed in the treatment of fistula, including: (1) thorough examination of the patient; (2) good exposure; (3) saucerising the edge of the fistula; (4) removal of scar tissue; (5) usually no separation of vagina from bladder; (6) use of silver wire or some other inert material; (7) closure in one layer without tension, making relief incisions if necessary; (8) continuous bladder drainage by a catheter so placed through the urethra or through a cystotomy incision that it does not put pressure on the suture lines.

The great difficulty in dealing with fistulas which follow radiation therapy is the avascularity of the tissues and the fixation and fibrosis of surrounding structures. It is essential in the operation to use tissues with a blood supply sufficiently good to insure healing, and this often means closure of the vagina well below the level of the fistula. The treatment of post-irradiation fistulas presents numerous difficulties, one of the severest of which is the presence of both a vesical and rectal fistula. One such case was treated by performing the following steps: (1) colostomy; (2) closure of the rectovaginal fistula; (3) closure of the vesicovaginal fistula by partial colpocleisis; and (4) closure of the colostomy.

(This paper will be of interest since postradiation fistulas are being noted from time to time in most large clinics. As the author states, the great difficulty in the closure of such fistulas is the avascularity, and in certain locations, the fixation or inaccessibility of the tissues. It is to be remembered that small fistulas of this sort, especially the rectovaginal type, may close spontaneously, as I saw in a recent case. When somewhat larger, closure will be promoted by temporary colostomy. In spite of the avascularity of the tissues, it is often remarkable how kindly they often heal, if there is no tension on the sutures. The latter is of prime importance, and, in my limited experience with vesicovaginal fistulas of this etiology, tension can be most easily avoided by free mobilization of the bladder. This involves separation of the vagina from the bladder, against which Russell seems to warn, although it would seem to me to be more frequently an advantage rather than a disadvantage.—Ed.)

ovarian pregnancies go to term than do tubal pregnancies. The exact diagnosis remains obscure in many cases until the pathological specimen is studied.

(The comparative rarity of ovarian pregnancy, of which this appears to be an authentic case, is of interest in view of the fact that large numbers of spermatozoa undoubtedly pass out from the tube into the pelvic cavity and on to the surface of the ovary. The only rational explanation is that the ovum, as it exists in the ovary and also for a brief span after extrusion, is not fertilizable because maturation changes have not been completed. While the first polar body is thought to be often given off in the ovary, the second is not extruded until the outer portion of the tube is reached. But the occasional occurrence of true ovarian pregnancy is clear enough proof that in at least some cases maturation changes are completed in the ovary.

In the study of removed specimens it is not always easy to decide whether an ectopic pregnancy mass, with often large masses of adherent blood clot, is ovarian or primarily tubal. Even when one feels strongly that the former is the case, it may be difficult to establish this beyond doubt through demonstration of the Spiegelberg criteria which have for many years, and quite properly, been considered essential for establishment of the diagnosis.—Ed.)

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OPERATIVE GYNECOLOGY

VAGINAL HYSTERECTOMY FOR CANCER OF THE UTERUS AND VAGINA

J. TRAPL

Charles University, Prague, Czechoslovakia

J. Obst. & Gynaec. Brit. Emp., **55**: 303-308 (June) 1948

The author has reviewed briefly the historical background of surgery in cancer of the uterus and vagina, and points out the two major types of approach to vaginal hysterectomy, namely, the anterior and posterior approaches. The aim of such operations is to remove the whole of the uterus, a sufficient part of the upper vagina and, most important, as much of the paravaginal and parauterine tissue as possible. The writer has developed a radical vaginal hysterectomy in which he uses the posterior approach and in this paper he describes his procedure in detail.

Preoperatively, the tumor is curetted and cauterized to prevent infection and implantation of tumor cells. The vagina and surrounding tissues are disinfected with tincture of iodine and silver nitrate. The operative field is infiltrated with procaine-adrenaline solution, a procedure which both aids dissection and renders the field bloodless. A transverse semicircular incision is made 2 cm. posterior to the frenulum and extending to the level of the ischial tuberosities, and the rectovaginal space is penetrated by blunt dissection. The "rectovaginal muscle" must be cut. The posterior vaginal wall is cut through sagittally to the level at which the vagina will be removed, and from the end of this incision a circular incision is made around the entire vagina. The wall of the vagina is freed about $\frac{3}{4}$ inch upward from the urethra, bladder and rectum and the vaginal cuff is closed with silk stitches through the anterior and posterior vaginal walls. By then cutting through the posterior and lateral parametrial tissues, the whole uterovaginal tract can be brought down and the dissection of the bladder and ureters facilitated. Using the finger or a swab, dissection is carried out along the edge to inner surface of the levators, displacing the rectum, vagina and bladder from the pelvic wall. The extraperitoneal fibers of the uterosacral ligaments are exposed and then separated as close to the rectum and lateral pelvic wall as possible by sharp dissection. The pouch of Douglas is then opened and the peritoneal portions of the uterosacral ligaments are cut through. The cardinal ligament is then freed, taking care to avoid the ureters, and is ligated close to the lateral pelvic wall; then the ligament is incised. The uterine artery is identified and ligated. The bladder is then dissected from the vaginal wall, blunt dissection being used for the uterovesical space and sharp dissection for the extraperitoneal and peritoneal portions of the uterovesical ligament. The lateral parametria, broad ligament and infundibulo-pelvic ligaments are then drawn taut by traction

and incised. The peritoneum is carefully closed, the bladder is fixed proximally and the rectum is covered by the edges of the levator. The remaining space is packed with iodoform gauze. Postoperatively, a catheter is left in place for 4 to 5 days and the iodoform gauze is removed gradually from the fifth to tenth day.

The author reviews the cases which he has operated in the last 25 years for cancer of the uterus, cervix and vagina. He has used the vaginal approach in 135 cases of carcinoma of the uterine corpus with a 1.48 per cent initial mortality, and in 8 cases of primary carcinoma of the vagina with no initial mortality. In carcinoma of the cervix, he compares 123 patients who received the vaginal approach with 179 cases having the Wertheim operation. All grades of carcinoma were treated and the percentage of cures after 5 years was 25 in the first group and 10.3 in the second. In general, the writer feels that the radical vaginal approach is a worthwhile procedure because of the low immediate mortality and morbidity. The one real objection is the impossibility of picking out and removing completely the iliac lymph glands which may be a site for metastatic lesions. 12 figures.

(Even in these days of revived interest in radical operations for a limited group of cervical cancer cases, I question whether Trapl's paper will excite much interest, since the concept of radical operation has again come to carry with it, as it did in the early days of the original Wertheim operation, the belief that extensive pelvic gland excision is an essential part of any radical operation. Even before the advent of radium, most operators, dismayed at the then high primary mortality, had retreated to the so-called modified Wertheim, including in this panhysterectomy, bilateral salpingo-oophorectomy, removal of a large vaginal cuff, and excision of as much parametrium as possible.)

The modified Wertheim procedure which many gynecologists adopted in this country, and which even during the era of radiotherapy has continued to be the operative method in selected early cases in a good many clinics, can legitimately be contrasted with the vaginal radical operation devised by Schauta, and widely practiced in most continental clinics, especially in Germany. I have seen this operation done many times in the German clinics, in Vienna and in Budapest. To be perfectly frank, I wondered why it had never obtained a foothold in American clinics. It permits of removal of any amount of vagina and excision of at least as much parametrium as can be obtained from above, with probably less danger to the ureters, which can usually be well visualized and displaced upward. And the salvage rates reported from the operation were definitely comparable to those reported from our own clinics following the modified Wertheim procedure.

The glaring defect of the Schauta operation, in the minds of those in our own country who have recently returned to radical surgery with increasing frequency in the past few years, is that it does not permit of radical gland excision, and hence my opening remark that Trapl's paper will probably not make any converts in this country, so far as operation for cervical cancer is concerned.

On the other hand, it still contains food for thought as regards cancer of the vagina, which in this country has been most frequently treated radiotherapeutically, with sometimes fairly wide but still inadequate local excision. The technic described by Trapl for the radical removal of the vagina permits of complete excision of that organ, together with the uterus and adnexa. It still has the shortcoming of not providing for complete gland excision, though the newer plans of extraperitoneal gland excision could well be utilized as supplementary procedures. Formidable as such a plan may be, it would probably not daunt some of the bold souls who, like Brunschwig, are doing pelvic evisceration for advanced cervical cancer.—Ed.)

VAGINAL HYSTERECTOMY: A REPORT OF 800 CASES

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Quart. Bull. Northwestern Med. School, 22: 300-302 (Fall) 1948

A series of 800 cases of vaginal hysterectomy is reported. Frequently more than one indication for the operation existed but the cases were grouped under the major indication for study.

Menorrhagia was the chief indication in 169 patients, the majority of whom were in the menopause. Myoma, relaxed outlets and unhealthy cervixes were associated with bleeding. The serious effect on ovarian activity had caused radium to be abandoned as a satisfactory method of treatment except in a few elderly women.

Myoma was the principal indication in 182 cases. Cystocele or rectocele was often present. Large tumors can be removed vaginally by morcellation. Intra-ligamentous tumors or those which have grown into the subvesical space or which are associated with pelvic inflammation are best removed from above.

Retrodisplacement which causes difficulty in an elderly woman is often treated satisfactorily by a hysterectomy and this can usually be done vaginally.

Descensus was the reason for operation in 333 cases. The necessary reconstruction of uterine supports can be done most satisfactorily from below.

Contraindications to vaginal hysterectomy are found in cases where previous surgery or pelvic inflammatory disease may have left adhesions. Corpus carcinoma is best handled by the abdominal route. Ovarian tumors of moderate size can be removed vaginally but such cases are better handled by laparotomy also. Nulliparity need not be a contraindication if the uterus is freely movable.

The method of operation varies with the type of case. Two general types are found: those in which simple uterine removal is needed and those in which restoration of supports for descensus is needed. A narrow right angled retractor for use under the bladder and a narrow curved retractor for use laterally are essential. The authors comment upon a few practical points of technique. The uterus is usually removed posteriorly and amputation of the cervix often facilitates removal. Methods of dealing with descensus and stress incontinence are described.

In the series of 800 cases there was one death from pneumonia and pelvic infection. Thus a mortality rate of 0.117 per cent is established for comparison with a rate of 0.4 per cent in 500 total abdominal hysterectomies. The morbidity in the last 540 cases was 20.3 per cent, based on a temperature reading of 100.4 F. for any 2 days.

A few injuries of the urinary tract were seen. The bladder was opened 5 times; 4 times closure was done immediately and in 1 case the fistula was closed some months later. In 2 cases the urethra was injured; repair in both cases was successful.

The authors feel that vaginal hysterectomy should be a part of the operative repertory of all gynecological clinics. With a careful selection of cases and an adequate familiarity with the technique, the operation can be a safe and useful one.

(The senior author of this paper has long been an exponent of vaginal hysterectomy, although he appreciates that in certain cases the abdominal route is to be preferred. This will be evident from the list of contraindications which he enumerates. The low mortality and morbidity rates shown in his large series are above criticism.

After all, regardless of proper indications, whether or not a man is going to be very partial to the vaginal or to the abdominal route is going to depend not a little upon his training. The Chicago school of gynecologists, under the influence of such men as Heaney and Danforth, has been partial to the vaginal route in cases in which either route gives good results and is therefore fully justifiable, while the abdominal route is the one of predilection in probably the majority of Eastern clinics. In the latter, the vaginal method is likely to be chosen chiefly for cases in which hysterectomy is desirable and in which there is marked prolapse of the uterus and bladder. Certainly in these the indication is a rather ideal one, giving an opportunity for convenient and easy correction of the cystocele in combination with a vaginal hysterectomy, which under such circumstances is likely to be very easy. In these clinics, however, the vaginal route is not often employed in cases in which there is no prolapse, much less in nulliparous women. Those who have seen the Chicago School at work, and they have now many disciples in other clinics, know that they often make vaginal hysterectomy seem very simple in cases in which this route would be viewed with misgiving by the customarily abdominal hysterectomist. The simple truth is that a well-trained gynecologist should master both technics, fitting the operation to the individual indications of each case. Even so, I suppose it is more or less inevitable that he will display some partiality in making his decision.—Ed.)

A CASE OF FIBROID IN THE CERVICAL STUMP AFTER SUBTOTAL HYSTERECTOMY

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J. Obst. & Gynaec. Brit. Emp., 55: 337, (June) 1948

A case is presented of a 37-year-old female who had had a subtotal hysterectomy with removal of the appendages 6 years previously, and it was noted at that time that there was difficulty in freeing the appendages. Her present complaint was vaginal hemorrhage of 24 hours' duration associated with a profuse discharge. On examination a solid tumor was found extending from the pubes upward to the umbilicus and lying somewhat obliquely in the abdomen. It was attached to the cervix, and this structure was displaced upward and to the right. A laparotomy was performed and the tumor was found to be a cervical fibroid which was enucleated without difficulty. The specimen weighed 9 pounds and was typical grossly and microscopically. The patient made an uneventful recovery.

The author was able to find only 6 previous cases of this condition in a review

of the literature. In 3 of these cases, one ovary had been conserved at the time of operation and in the remaining cases ovarian tissue may have been left in inflammatory adhesions. It was felt that conservation of ovarian tissue would favor the development of a fibroid tumor in the cervical stump. The fact that these tumors reach a large size in a relatively short time might possibly be the result of early degenerative changes consequent to poor blood supply or they might owe their rapid growth to low grade malignant changes.

(This report, by one of England's leading gynecologists, presents a number of interesting features. If a supravaginal hysterectomy is done for multiple myomas, it is easy enough to see how a small tumor nodule can be inadvertently overlooked below the line of amputation. I have more than once almost done this, noticing the residual nodule only when the cervical stump was brought up for suspension or perhaps when it was about to be peritonealized. I have no doubt that others have had the same experience, though it must be far less frequent in these days of total hysterectomy than when the subtotal technic was the prevailing one.

We have all believed and taught that myomas will not grow and will commonly diminish in size after the menopause, whether natural or surgical. In Gemmell's case the appendages are said to have been removed at the original operation, and yet 6 years later a myoma in the residual cervix had grown to the size of 9 pounds. An isolated case of this sort just can't mean that our previous views on the fate of myomas after the menopause are all wrong. There are several possibilities by way of explanation. The author reports that at the original operation there was difficulty in freeing the appendages, and even the most expert operator may leave behind some ovarian tissue in these technically difficult cases. Again, as he himself suggests, degenerative changes may lead to postmenopausal increase in the size of myomas, though this could scarcely have explained an increase to 9 pounds, and would have been noted both grossly and microscopically. Finally, rapid postmenopausal growth of myomas must always lead to the suspicion of sarcomatous change, even though it be of low grade histologically. Presumably no such change was found in the microscopic examination of Gemmell's case, though it must be remembered that it has been often missed even when many blocks are examined, as is illustrated by the reported cases of "recurrent fibroids" in which the sarcoma was not histologically demonstrable until perhaps after several recurrences.—Ed.)

THE FREQUENCY OF HYSTERECTOMY FOR BENIGN DISEASE

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Pennsylvania M. J., 51: 993-997 (June) 1948

A study was made of the incidence of hysterectomy, in which only varying degrees of uterine fibrosis or no evidence of pathology was found, in a series of 1000 specimens submitted for pathological study during a period of 34½ months.

Hysterectomy was performed in 26 per cent of all pelvic operations. Of the 1000 specimens, 17.5 per cent showed little histologic abnormality in the removed

tissues. There were 175 of these patients; 47 per cent complained of abnormal vaginal bleeding and 31 per cent complained of abdominal pain. Of the group 69.5 per cent were between 31 and 55 years of age. In 60 per cent of these patients ovarian tissue was not conserved. There was 1 death and 15 per cent morbidity in these 175 patients. 2 figures.

(I do not believe that any honest and fair-minded gynecologist would deny the fact that far more hysterectomies are performed throughout the country than are justified, any more than any of us would deny that more operations in general are done than are necessary or justified. No one has more strongly emphasized the frequent abuse of hysterectomy than Norman F. Miller, in his paper entitled "Hysterectomy—Therapeutic Necessity or Surgical Racket" (*Am. J. Obst. & Gynec.* 51: 804, 1946). To this the interested reader may be referred. The subject has been previously commented upon in these columns. Clear as the abuse is, it is obvious that the pathological laboratory can not in all cases be the arbiter of the justifiability or unjustifiability of removing the uterus. For example, many gynecologists quite conscientiously and justifiably remove the normal uterus vaginally in certain cases of prolapse, and many other examples could be mentioned. But the correctness of the general thesis still remains unshaken.—Ed.)

FOUR CASES OF INTERSTITIAL PREGNANCY FOLLOWING HOMOLATERAL SALPINGECTOMY

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Am. J. Obst. & Gynec., 56: 574–578, 1948

The writer presents 4 cases of interstitial pregnancy following homolateral salpingectomy. This condition is extremely rare, only 25 cases having appeared in the literature previous to the present report.

The second case reported in this paper had 2 cornual pregnancies on the same side preceded by a homolateral salpingectomy. No similar case has previously been reported. The fourth case in this report is included because it was primarily cornual and secondarily intraligamentous.

The most probable explanation of this occurrence is external migration of the ovum to the interstitial portion of the tube that has regained its patency. Convincing evidence is presented for external migration of the ovum, whereas such evidence is lacking for internal migration in humans. Incomplete removal of the cornual portion of the tube and regeneration of the tube may be contributing factors in the renewed patency of the tube.

(In all 4 of the cases reported by the author, a reading of the histories indicates that the operations previously performed were not simple salpingectomies, but salpingo-oophorectomies. I mention this because it has a bearing on the explanation of the interstitial pregnancies which occurred subsequently on the operated side. Were only the tube removed, the fertilized ovum would be expected to have its source in the conserved ovary of the operated side; but where both tube and ovary have been removed, the only possible

source is the contralateral ovary, and the lodgment of the egg in the interstitial portion of the removed tube must be by external migration. This, after all, is a well established possibility, a good many pregnancies having been noted after removal of one ovary and the contralateral tube, as I myself have observed. On the other hand, I know of no evidence to indicate that internal migration, which undoubtedly does occur in certain animals with bicornate uteri, has ever occurred in the human female.

Finally, it is necessary, if one invokes external migration as the responsible mechanism in cases of the type described by Frankel, also to assume that the stump of the removed tube regains its patency, but for this possibility there is ample proof. Sampson, in his studies of tubal stumps, showed that the endosalpinx often becomes markedly proliferative, growing out to the peritoneal surface and sometimes undergoing an endometrial metaplastic transformation. Again, a frequent method of tubal sterilization, before the present day popularity of the Madelener and Pomeroy technics, was bilateral cornual resection of the isthmic portion of the tubes, but failures were not infrequently noted. These could not be explained except on the basis of recanalization of the proximal tubal stump.—Ed.)

STERILITY

FACTS AND FANTASY IN THE STUDY OF FEMALE INFERTILITY

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J. Obst. & Gynaec. Brit. Emp., 55: 171-180 (April) 1948

In this review of female infertility, the author studies the first 1,000 cases investigated at the Fertility Clinic at Oxford. They consist of 729 nulliparous women and 271 who complained of an acquired sterility.

The need for premarital advice on matters of sex and for marriage guidance is emphasized by the fact that 4 to 5 per cent of a series of married women complaining of infertility were found to be virgins. The author notes that to give advice on such matters is more time-consuming and less dramatic than to perform plastic operations on already disorganized Fallopian tubes, but because of the need for the one and the poor results from the other we should try to keep a sense of proportion and recognize where there is the greater need.

It should be remembered that unfortunately every woman who desires to conceive should not be encouraged to do so. It is important that a careful medical examination precede the investigation of infertility.

In the author's series of 1,000 cases, at the first examination it was found that defective male secretion was present in 35 per cent of the men and defective ovulation in 28 per cent of the women examined. It is noted that defect in either male secretion or ovulation was frequently of temporary duration and that the corrected figures after repeated examinations would be much lower.

Reference to the results published by other workers shows that the incidence of complete tubal occlusion varied from 26 to 50 per cent. In the author's series the incidence of apparent lockage was 21.6 per cent, but by the use of spasmolytics such as nitroglycerine it is shown that the incidence can be reduced to 12.8 per cent, and in a smaller series of 171 patients investigated at the end of the series the apparent rate was 9 per cent. The writer suggests that even this rate of 9 to 12 per cent is probably too high, and it included patients with apparent occlusion due to uterotubal irritability unrelieved even by nitroglycerine.

On the above figures, the author claims that unless effective steps are taken to relieve hitherto unsuspected uterotubal irritability, the results of the infertility test and lipiodol investigation are likely to have at least 100 per cent error.

A detailed study of 111 patients in whom the uterus and Fallopian tubes were investigated under the fluoroscope indicated that probably the most common cause of unilateral uterotubal blockage is the lack of synchronization of waves of contraction originating at the uterine cornua. Several of the 111 patients had repeat tests made at a later date, and it was found that either both tubes were

now patent or the opposite tube was now patent and the original one apparently blocked.

The author states that the female genital tract is the most "hysterical" portion of a woman's anatomy. It is under both nervous and hormonal control, a fact sometimes forgotten in these days of hormonal emphasis. Autonomic disharmony manifested elsewhere is responsible for duodenal spasm, vascular spasm, gastric stenosis and other similar disorders. It is suggested that uterine irritability may not only be a factor in sterility, but also in the causation of repeated abortions. 7 figures.

(The author of this paper, one of the best known gynecologists in England, is well qualified to appraise the problem of infertility, and he does so very well in this paper. While the married virgin is not a rarity, I would not have thought that she makes up as much as 4 to 5 per cent of our infertile patients, and this has certainly not been my own experience. Most infertile patients do not consult the physician for a year or more after marriage, and even though complete coitus is not accomplished for a considerable time, perseverance often then wins out. But it is surprising how many years both partners will in some instances put up with this hymenal barrier to a full wedded life. Not always, however, is infertility a result, as every gynecologist has seen cases of pregnancy in both single and married women who have intact hymens. Some years ago I saw a woman, married 10 years, in whom the hymen was intact and rigid, but who nevertheless was several months pregnant. An enterprising spermatozoon will often travel far and overcome many obstacles to keep his tryst with the ovum.

The author wisely cautions against conclusions concerning tubal patency or nonpatency on the basis of single insufflations. No woman should be convicted of nonpatency on the basis of a single test, and repetitions of the test should always be done, with often surprisingly different results. The use of spasmolytics is sometimes the explanation, but not always. The author's belief that unilateral blockage most often due to lack of synchronization of contraction waves may possibly be correct, though it will stand a bit of confirmation.

Since the word "hysteria" is derived from the Greek word for uterus, the author is evidently not the first to consider this organ the most "hysterical" portion of a woman's anatomy. He suggests that sterility or repeated abortion may be produced by the "hysterical" uterus. On the other hand, to illustrate the contrariness of females, there are some who become hysterical if pregnancy occurs.—Ed.)

THE CLINICAL EVALUATION OF HYALURONIDASE IN HUMAN INFERTILITY

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Am. J. Clin. Path., 18: 491-498 (June) 1948

Hyaluronidase is an enzyme elaborated by the testicle and certain other organs and bacteria which produce depolymerization and hycolysis of hyaluronic acid. The substrate has as its function the holding together of cells in a jelly-like matrix. The viscous gel in which the follicle cells of the cumulus oophorus are im-

bedded contains hyaluronic acid complex. Dissolution of this cellular barrier around the ovum is necessary for fertilization and is probably brought about by hyaluronidase. The concentration of hyaluronidase in semen parallels the sperm count. The seminal vesicle apparently plays a role in the production of this enzyme and the concentration of hyaluronidase in the semen is increased after the semen leaves the seminal vesicle.

Hyaluronidase was found to be of therapeutic value in human infertility in 33 of 102 selected patients. The application of the enzyme may be of value in the following instances: (a) In patients presenting sperm concentrations of less than 50 million per cc., because the enzyme is usually absent when the sperm population is below this level. (b) In patients presenting a normal sperm concentration (above 100 million per cc.), where the enzyme concentration is low, that is, less than 1 unit, as determined by the author's method. (c) Occasionally in patients with normal sperm counts and adequate hyaluronidase in whom no adequate reason can be found for infertility.

The author has shown that hyaluronidase and the enzyme that liquefies cervical mucus, when given in conjunction with hyaluronidase, may be of distinct value in patients with nonspecific endocervicitis. Sexual abstinence for a limited period (average about 2 weeks) had no effect on the hyaluronidase content of the semen.

The main difficulty encountered with this form of treatment was the determination of the best time for application of the hyaluronidase to the cervical canal. It should be given at the time of ovulation but this is not always possible. Additional studies by the author concerning self-insertion of material containing the enzyme are now in progress.

(The recent interest in the enzyme known as hyaluronidase is of interest, but it is too early to know whether or not it will add anything of real value in the management of our sterility problems. The scattered and meager early reports do not make one feel very optimistic.—Ed.)

HYSTEOSALPINGOGRAPHY EMPLOYING A WATER-SOLUBLE CONTRAST MEDIUM

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J. Obst. & Gynaec. Brit. Emp., 55: 270-272 (June) 1948

It is the author's contention that any radio-opaque substance used in testing the patency of the Fallopian tubes must fulfill certain criteria. It is submitted that these criteria are: ease of introduction, easy visibility under the screen, non-irritability to the epithelium of the Fallopian tubes and peritoneum, and rapid absorption from the tubes and peritoneum. The writer has used "Pyelosil", a 35 per cent solution of the diethanolamine salt of 3:5 di-iodo-4-pyridone-N-acetic acid, and it appears to fulfill all of the above criteria.

A minimum amount of force is needed to introduce this solution into the uterus and tubes and it is readily visualized on the fluorescent screen. Absorption is rapid and is usually complete within one hour. Excretion occurs via the urinary tract. There has been no evidence of local irritation, and spasm of the ampullary end of the tube occurred in only one case in this series.

Twenty-four infertile women have been subjected to hysterosalpingography using "Pyelosil" and 5 cases of obstruction were demonstrated. Two of these were due to pyosalpinx, one due to tuberculous salpingitis, and in 2 cases the cause was undetermined. No therapeutic benefit is claimed in the use of "Pyelosil" in the investigation of tubal patency. 4 figures.

(I do not know of anyone in our own country who has used this particular preparation in hysterosalpingographic studies, although it would certainly seem that water-soluble contrast media offer definite advantages over the oily media which have been so widely employed. Hysterosalpingography is by some employed almost routinely in sterility studies, while others use it rarely, feeling that all the requisite information of practical value can be obtained by the simpler, safer and less expensive method of tubal insufflation with carbon dioxide. I myself happen to belong to the latter school.—Ed.)

THE PROBLEM OF INFERTILITY

B. SOLOMONS

Dublin, Ireland

Brit. Med. J., 2: 90 (July 10) 1948

A discussion was presented on infertility and its treatment. The author regarded sterility and impaired fertility as synonymous terms and considered a marriage sterile if conception had not taken place after 2 years. He felt that male infertility was responsible in 50% of the cases. A plea was made for the recording of deaths due to tubal insufflation. The use of opaque fluids in such diagnosis and treatment was recommended as no fatality had occurred with their use in a large series of cases. Operations on the Fallopian tubes had been only 10% successful.

Mr. Sharman stated that there had been no deaths as a result of insufflation with carbon dioxide done on 3,000 cases.

Mr. Wather discussed the transportation of sperm to ovum. Ejaculation, motility and penetration were important factors. The quality of the sperm was more important than the quantity.

Mr. Malpas discussed recurrent abortion. He felt that emotional shocks were the most common cause of abortion in healthy pregnancies.

Mr. Binney, Barrister at Law, discussed the legal position of the child in artificial insemination.

(I do not believe that sterility and impaired fertility are exactly synonymous terms. Solomons, who is known to many Americans from his visits here and who is a former Master

of the Rotunda Hospital in Dublin, evidently prefers salpingography to tubal insufflation, but if he bases his preference on relative death rates, it would seem that he is on shaky grounds. So far as I know, there is no recorded death from embolism following tubal insufflation, when carbon dioxide and not air was used, as should always be the case. On the other hand, quite a group of cases of embolism, including a few fatalities, have been reported after oil injections of the tube.

Mr. Watkins' statement that the quality of the spermatozoa is more important than the quantity can be endorsed. Although there is some degree of parallelism between the two, this is by no means absolute. Finally, I am inclined to believe that most of us would doubt the correctness of Mr. Malpas' statement that emotional shocks are the most common cause of abortion in healthy pregnancies.—Ed.)

AN EVALUATION OF INFERTILITY FACTORS

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California Med., 69: 32-36 (July) 1948

The 5 principal factors which play an etiologic role in infertility are discussed and an attempt is made to point out their relative importance.

The coital factor can be studied by a searching coital history, plus a post-coital Huhner test. The role of the psychosomatic factors in infertility is not well understood.

The male factor does not receive the attention it should even now. The incidence of this factor in infertile couples is between 30 and 40 per cent. A really adequate and accurate sperm analysis must be done.

The tubal factor plays a major role in 40 to 50 per cent of all cases. Either tubal insufflation or hysterosalpingogram contains a 10 per cent error and decisions should not be made on the basis of the single use of either.

The author feels that too much attention can be given to anovulation and to mild endocrine dysfunction as a part of the female endocrine factor.

The importance of the cervical and vaginal factors is stressed and the value of a pre-coital Ringer-glucose douche is mentioned. A plea is made for more careful inspection of the cervix and a more standardized technique for the Huhner test.

Even if an ejaculation specimen of semen is competently examined and a Huhner test done, other masculine factors may still have to be reckoned with. Normally motile spermatozoa are not necessarily potent from the standpoint of fertilizing capacity, just as, even in the ovulating woman, the ovum may not be fertilizable because of what we have come to speak of as deficiency of germ plasm. This is a very intangible factor, but there is good reason to believe that it is often important. When the deficiency in either male or female germ cells is less marked, conception occurs, but often with early spontaneous abortion, sometimes repeatedly. That bad eggs or bad sperm are the responsible factors has received support from the microscopic examination of the conceptuses in such cases, this showing abnormalities in a large proportion, as Mall and various other embryologists have demonstrated.

A considerable proportion of the sterility cases which I see have been studied previously in other clinics. Most of them have had the ordinary investigations, such as tubal insufflation, endometrial biopsy, examination of the husband's semen, and basal metabolism studies of the wife, but most often not of the husband. The latter, indeed, seems to me the point which is most likely to be overlooked in otherwise adequate investigations, and it not infrequently shows marked thyroid deficiency. I mention this because, while no one knows much about the undoubted relations between the thyroid and the reproductive function, it does seem, on purely clinical grounds, that the thyroid is in some way linked up with that intangible germ plasm factor I mentioned above. There are few experienced gynecologists who would not agree that, empirical as it is in the present state of our knowledge, thyroid therapy is probably the most important hormonal adjunct in the management of infertility.

The author's feeling that anovulation and mild endocrine dysfunction receive too much attention is applicable chiefly to those who seem to think that infertility calls for magic "shots" of some hormone or another with no adequate consideration of other and often far more important factors. On the other hand, such endocrine considerations should form a part of the adequate study of such cases. Unfortunately, in the case of anovulatory cycles, even when these are demonstrated, there still remains the discouraging question of what to do about it. But that is a story in itself.—Ed.)

MISCELLANEOUS

THE PRESENT POSITION OF NEUROSURGERY IN GYNAECOLOGY

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Brit. M. J., 2: 585 (Sept. 25) 1948

The advent of autonomic surgery 20 years ago marked an epoch in gynecology, and since that time a variety of operations, mainly designed to interrupt sympathetic pathways from the uterus, but all concerned with the relief of pelvic pain, have been carried out. The operations which have survived the initial enthusiasm are presacral, ovarian and uterosacral sympathectomy, cordotomy, pelvic alcohol block and various types of spinal injection.

Resection of the presacral bundle accomplishes almost complete denervation of the uterine musculature. The sympathetic nerves to the uterus carry motor contractile fibers so that their section diminishes the muscular spasm which is the basic cause of spasmodic dysmenorrhea. This procedure is indicated in severe dysmenorrhea and certain other conditions such as pelvic carcinoma, where long-standing pain is a prominent symptom. The operative technique is relatively simple and quite safe, provided careful attention is paid to the anatomical relations of the area. The results in spasmodic dysmenorrhea have been very favorable, with some series reporting 100 per cent cures. The author's own experience has been an increasing rate of cures as he gained experience with the procedure and with the selection of his cases. In the last 3 years he has had only one case which was not entirely relieved of pain. His total series covers 86 cases over a period of 16 years. In secondary dysmenorrhea this operation is less successful, and it should not be undertaken without correction of other pelvic pathology.

The visceral pain of incurable pelvic carcinoma may be relieved by the above operation, though the spinal pain, often predominant, naturally remains unaffected. The author's own experience in such cases has not been encouraging, and in 8 cases only 2 were definitely improved.

In some cases of dysmenorrhea, the cause of the pain is ovarian and section of the ovarian nerves has been advocated. It has also been successfully applied to cases of severe ovulalgia and as a palliative measure in ovarian endometriosis. There is no doubt of the value of this operation in certain carefully selected cases but the author points out that by sectioning the main vascular and nerve supply to the ovary its function may be altered. It should therefore never be undertaken in young nonparous women, except for the most urgent indications.

Alcohol injection of the pelvic plexus has been used with success in spasmodic dysmenorrhea. It is used in combination with cervical dilatation, the main advantage being the simplicity of the technique. It may also be of value in painful

parametritis and vaginal neuralgia. Of 61 cases reviewed by Davis, 70 per cent were permanently and adequately relieved of severe dysmenorrhea and 18 per cent were improved.

Intrathecal alcohol injection has been used with some benefit in cases of incurable cervical carcinoma. The method is an extremely easy one, requiring the minimum of preparation and apparatus but it carries several disadvantages such as incontinence of feces and urine and other paralytic complications. Despite these complications, the relief when obtained is gratifying and the author feels that it is a worthy procedure. Magnesium sulfate has been substituted for alcohol by some investigators but early reports have not been too encouraging.

Section of the uterosacral ligaments may be indicated in the so-called "posterior parametritis syndrome." This procedure, the original pelvic sympathectomy, fell into disrepute because of the complications encountered. However, recently it has been revised and improved and some benefits are obtained from it in painful pelvic disorders. Although the author's results with resection of the uterosacral ligament have been unsatisfactory, he feels that theoretically it is a sound procedure and deserves further study. Uterosacral alcohol injection is a good though temporary substitute for resection and is useful as an adjunct to other procedures.

Epidural and paravertebral blocks are of value when temporary relief of pain is desired. The main indication for paravertebral block would seem to be in the determination of whether pain is of visceral origin or not. If the pain is relieved, it will very likely be permanently relieved by presacral neurectomy.

Cordotomy, one of the earliest of neurosurgical procedures in gynecology, involves a very tedious operation and is probably indicated in only a very few cases.

(This paper reviews the subject very nicely, although I am inclined to believe that Davis' results from the employment of presacral sympathectomy are more consistently good than the 60 to 70 per cent of cures reported by most gynecologists in our own country. This operation has established itself as a valuable one in the comparatively small proportion of severe dysmenorrhea cases in which nonsurgical treatment will not give sufficient relief from the pain. As I have previously mentioned in these columns, the operation is often a valuable supplementary procedure when the primary indication is some such condition as endometriosis, especially in young women. In this group the operation is usually of conservative type, and aberrant endometrium may be left behind, in the uterosacral ligaments or elsewhere. The surgeon can therefore not always be sure that the primary operation will give relief from the dysmenorrhea, and presacral sympathectomy is a rational adjunct in such cases. I do not believe that section of the ovarian nerves for cases of supposed ovarian pain is as rational or as well established a procedure as presacral resection.

The problem of mitigating the suffering of the advanced cancer patient is still a distressing one. The severe pain in these cases is usually due to infiltration of the pelvic nerve sheaths, and there would seem to be little hope for relief from presacral neurectomy. Subarachnoid alcohol injection should be more helpful, but it has disadvantages, some of which the author mentions. Cordotomy, which has been advocated by some neurosurgeons, is too formidable a procedure on a debilitated patient who cannot expect to live much longer. As a matter of fact, the vast majority of cancer patients are let down as gently as possible through the use of pain-relieving drugs, usually including morphine.—Ed.)

THE USE OF THE "PHASE-CONTRAST" MICROSCOPE IN
CLINICAL GYNAECOLOGY

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J. Obst. & Gynaec. Brit. Emp., 55: 261-267 (June) 1948

The phase-contrast microscope, a recent innovation in microscopy, promises to be of great value in cytological investigations. Cells obtained by smear, pipette or scraping techniques may be studied immediately in the fresh state without stains and the cytoplasmic structure and nuclear characteristics may be seen with ease and clarity. Provided reliable criteria are established, the recognition of normal or malignant cell types requires no greater experience than that necessary for the diagnosis of stained paraffin sections.

The material to be studied is suspended in Ringer's solution and then examined promptly whenever possible. A single drop is placed on a glass slide, covered with a glass cover slip and sealed with vaseline. The movement of bacteria, shifting debris, undulations of cilia, shifting of cytoplasm and granular particles, in addition to the very rapid Brownian-like movements in certain cells, lead to a changing picture under the microscope and add to the difficulties of diagnosis by this method.

The authors state that it is not their intention to lay down specific features by which the identity of the various cells of the mucosal layers of the female genital tract can be established. However, they briefly review the histological patterns commonly encountered and illustrate the various cell types by photomicrographs. All cell types from squamous vaginal epithelium to the ciliated epithelium of the Fallopian tubes have been recognized. Malignant cells have been identified by the presence of mitotic figures, very large nuclei and binucleate forms, irregular granules and chromatin clumps with destruction and irregularity of the cell membranes. Within many malignant cells the movement of the granular particles is apparently haphazard and lacks the localization observed in normal cells. In some such cells numerous, small, translucent globules of fat are a prominent feature.

The authors feel that with further investigation and consequent elaboration of criteria essential to accurate diagnosis, this technique will be applied to the study and diagnosis of early exfoliative malignancies as well as to the less vital analysis of infections and hormonal disturbances as manifested in the gynecological tract. The main advantages of this method are the ease with which it may be performed and the rapidity with which it is completed. 29 figures.

(I am not sure just what a phase-contrast microscope is but I gather from the above abstract that the principle is much like that of examining thin bits of unstained tissue under the microscope, with a part of the illumination shut off. One cannot imagine that this method would give the clearness and detail possible with fixed and stained tissues, with full appreciation that such fixed and stained preparations do distort the cells somewhat.

On the other hand, for certain purposes the simple and apparently crude plan of examining fresh unfixed and unstained tissue does give surprisingly useful information. This was brought home to me when, many years ago, we were studying cilia in the tube, employing the so-called Nylander technic. A tiny bit of mucosa from a freshly removed tube is scraped or shaved off, put on a slide and a cover slip pressed down to make a very thin film of the epithelium. The thinner the film the better the results. Examining such a preparation under the high power, with the light partly cut off, gives one a different picture of the epithelium than one gets from the fixed and stained section. In the latter, the cilia are likely to be short and shrunken. In the fresh section they seem surprisingly long and active, lashing so violently that one might imagine that they could almost kick a football along, much less an ovum. I can well believe that the same general method, if one developed himself by long experience, might be of considerable supplementary value for special indications, although I feel sure that the authors would agree that it can never replace the laboratory technics in common use.—Ed.)

IS CHRONIC CYSTIC MASTITIS A PRECANCEROUS LESION? A TEN YEAR FOLLOW-UP STUDY OF TWENTY-SIX CASES

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Arch. Surg., 56: 338-344 (March) 1948

There is no unanimity of opinion in the literature concerning chronic cystic mastitis, its relation to cancer of the breast or the best method of treatment. Twenty-six cases of chronic cystic mastitis operated on prior to 1931 are used in a 10 year follow-up study and reported here.

Treatment in this hospital has been based on the histologic type of the lesion. Simple chronic mastitis, present in 80 per cent of the cases, is treated by local excision of the involved area and regular follow-up is regarded as unnecessary. Chronic cystic mastitis with papillary proliferation was present in 4 per cent of the cases and was treated by local removal and examination every 6 months. Chronic cystic mastitis with atypia comprised 15 per cent and simple mastectomy with regular follow-up was used. Carcinoma of the breast did not develop in a single instance. 3 figures.

(The author's series is much too small to be of statistical value, but the opinions he has formed conform to those held rather generally. While there has been some difference of opinion, the consensus among surgeons is that the simple cystic variety of chronic mastitis is not to be looked upon as a precancerous lesion. Like swiss-cheese hyperplasia of the endometrium the lesion is estrogen-induced, and these two conditions have many points in common. It is of interest that the gross appearance of the cut surface of a breast showing marked benign cystic change often has somewhat the same swiss-cheese pattern which characterizes endometrial hyperplasia microscopically. Like the benign hyperplasia of reproductive life, it appears to have no bearing on the development of cancer.

On the other hand, in the markedly proliferative types of chronic mastitis, with pronounced and often papillary intraductal overgrowth of epithelium, such as is to be seen in

the so-called Schimmelbusch disease, the majority of authors are inclined to accept a definitely precancerous hazard. When localized, simple but complete excision is usually adequate, but when widespread or multicentric, simple mastectomy may be indicated. In no other field is a knowledge of the gross pathology of more importance at the operating table, and in no other is the value of good frozen sections greater than in surgery of the breast.—Ed.)

USE OF RING PESSARIES

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Brit. Med. J., 2: 227 (July 24) 1948

In a series of 74 cases using ring pessaries, 57 underwent colporrhaphy or vaginal occlusion successfully and 14 rings were removed as unnecessary. Of the remaining 3 cases, 2 were unfit for operation and one preferred the ring. Thus 5 per cent of the pessaries seemed necessary.

There are 3 types of cases in which pessaries are generally fitted. The first is in the descent of the vaginal wall following childbirth in young women. The author feels that the use of the pessary here only aids in stretching the walls. The second type is that of the permanent descent of the vaginal walls in the middle-aged woman and is also undesirable, as no consideration is made of the degree of prolapse, stress incontinence, or condition of the cervix.

Only where operation is impossible does the author feel that there is any excuse for the use of the ring pessary.

(The lowly pessary receives scant consideration these days, and a large proportion of modern medical graduates have little or no knowledge as to the indications for its use, its mechanism, or its possible hazards. And yet it has a definite field of application, much larger than that indicated by the author, although his comments obviously pertain only to the ring type of pessary. If we extend our consideration to cover the Hodge-Smith type of pessary, the instrument is frequently of value in retrodisplacements of the uterus, especially those so often discovered at postpartum examination. When combined with knee-chest exercises, they often restore the uterus to normal position. Again, they may be of value in deciding whether or not a patient's backache is due to an existing retrodisplacement, and also as palliative treatment in the woman who for economic or other reasons is obliged to defer a corrective operation when this is indicated.)

The ring pessary finds its chief field of application in the management of prolapse where operation is declined or where the patient's age or infirmity makes this undesirable. I suppose there are few gynecologists who do not number among their patients a number of nice old ladies who have worn such pessaries for many years. The affection they form for these pessaries is touching and the idea of getting along without them would fill the patients with dismay. This is true even in women, not always of the older group, in whom pessaries were inserted years before by a "medical gynecologist" even though there was little or no prolapse or retrodisplacement. Such patients not infrequently become pessary addicts, getting a psychological rather than a uterine uplift from the little implement tucked away in the vagina. This is of course a misapplication of such mechanical therapy, and various others could be discussed if space permitted.

The care of the pessary is likewise important, including the necessity of removing and cleaning it at intervals of 2 or 3 months, and sooner, should it cause discomfort or bleeding. The literature contains many reports of the dangers of neglected pessaries, which have been allowed to remain for sometimes unbelievably long periods. I remember that the late Dr. Howard A. Kelly once removed at abdominal operation a pessary which had been inserted into the patient's vagina many years previously. I have seen a few cases in which the pessary had ulcerated through the vaginal wall and become completely or almost completely buried. The removal of such buried pessaries is not easily done, and one must be careful not to injure the bladder or rectum. A good plan is to bite through the pessary at various points with a bone cutting forceps, and then to slide the individual segments gently from the covered groove in which they are buried. As a matter of fact, an instrument somewhat resembling a bone cutting forceps was devised many years ago by a German gynecologist, Pivniczka, for just this purpose. It was called a pessariotome.

Despite these lurid possibilities in the grossly neglected cases, the fact remains, as stated at the outset, that there is still a definite though limited field for the vaginal pessary. I believe that most of the older school of gynecologists appreciate this fact, but I am not sure that it is sufficiently well recognized by the younger group.—Ed.)

AUTHOR INDEX

APRIL, 1949

- Asirvathan, J., 223
Assali, N. S., 232
- Baker, J. K., 289
Bender, S., 267
Black, E. F. E., 185
Blumer, C. E. M., 269
Bradbury, J. T., 187, 244, 247
Brown, J. A., 225
Brown, W. E., 187, 244, 247
Brown, W. W., 188
Brzezinski, A., 240
Burdman, M., 256
Burnside, A. F., 275
Burton-Brown, J. R. C., 200
- Cantarow, A., 246
Causey, G. C., 292
Chalmers, J. A., 285, 286
Chesley, L. C., 184
Chisholm, W. N., 196
Cole, H. H., 248
Corbet, R. M., 205
Cosgrove, S. A., 209
Cowie, D. B., 176
Culiner, A., 311
Curtis, A. H., 270
- Danforth, W. C., 298
Darling, M. A., 159
Davidsohn, I., 215
Davis, A., 309
de Soldenhoff, R., 282
De Meio, R. H., 246
Diamond, L. K., 214
Diddle, A. W., 256
D'Ingianni, V., 274
Dougal, D., 268
Douglas, R. G., 230
Drewes, E. L., 274
Dula, F. M., 258
- Eckman, P. F., 277
Edwards, J. L., 269
Ehrenberg, C. J., 224
Emge, L. A., 284
Evans, A. M., 266
- Flexner, L. B., 175, 176
Frankel, A. N., 301
Fraser, J., 218
- Gemmell, A. A., 299
Gluckman, J., 311
Goldberger, M., 254
Green, H. S. N., 280
Gregory, R., 227
- Hadley, J., 199
Haines, M., 289
Hall, P. O., 209
Hardie, M., 264
Hellman, L. M., 175, 176
Hobson, W., 180
Horne, E. O., 288
Hultquist, G., 205
Hunter, A. L., 222
- Igná, E. J., 159
Ingelman-Sundberg, A., 259
- Jakobowicz, R., 217
Jang, G., 207
Jefferiss, D., 305
Jennett, R. J., 188
Joffe, H. H., 277
- Kazmierski, R. H., 287
Kistner, R. W., 232
Knight, W. R., 291
Kraushaar, O. F., 187
Krieger, V. I., 217
Kullander, S., 194
Kurzrok, R., 304
- Lafferty, H. D., 300
Landesman, R., 230
Landowne, M., 189
Lapid, L. S., 254
Lesse, S., 202
Levin, W. C., 227
Livingstone, R. G., 253
- McCarter, J. C., 292
Meigs, J. V., 272
Mengert, W. F., 188

- Mino, R. A., 253
Mino, V. A., 253
Morton, J. H., 245
Mowbray, R., 201
Mueller, P. F., 197
Mustard, W. T., 218

Newton, B. L., 280
Novak, E., 192

Obermer, E., 178
Oliver, H. M., 288
Overstreet, E. W., 307

Paschkis, J. E., 246
Power, H. A., 204
Proctor, N. K., 175, 176

Racker, D. C., 257
Rae, I. P. F., 246
Rakoff, A. E., 241, 246
Reddington, M., 313
Redman, T. F., 279
Reed, H. L., 312
Reynolds, R. A., 298
Ries, R. G., 293
Ross, R. A., 252
Ruby, B., 189
Russell, B., 228
Russell, S., 295

Safford, H. B., 250

Saunders, C., 219
Schott, A., 195
Searle, W. N., 289
Shaw, W. F., 210
Silberblatt, W. B., 250
Simmons, R. T., 217
Slovin, I., 250
Smith, O. W., 190
Solomons, B., 306
Stallworthy, J., 303
Stern, K., 215
Stoll, W., 209

Thomas, G. B., 255
Thompson, W., 189
Tietze, C., 221
Trapl, J., 296
Trapp, E., 264

Villaverde, M., 243
Vosburgh, G. J., 175, 176

Walter, R. I., 254
Wells, A. H., 277
Wilde, W. S., 175, 176
Wittenberg, S. S., 293

Ylppö, A., 212

Zander, E. L., 274
Zondek, B., 240

Review

MODERN CONCEPTS OF CERVICAL CARCINOMA

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OUTLINE

Modern concepts of cervical carcinoma

	Page
History	
<i>Early History</i>	315
<i>History of the Operative Attack</i>	316
<i>History of Irradiation</i>	
Radium.....	318
Roentgen Therapy.....	318
Refinements of existing methods	
<i>Classification</i>	319
<i>Prophylaxis</i>	319
<i>Irradiation</i>	320
<i>Ancillary Operations</i>	320
<i>Lay Education</i>	320
<i>Summary</i>	320
Intraepithelial carcinoma.....	321
Exfoliative cytology.....	322
Revival of the operative attack.....	325
The future.....	326

HISTORY

Early History. Until the advent of cellular pathology, carcinoma of the uterine cervix was recognized only as an ulcerating and sloughing growth, undifferentiated from other exuberant, granulomatous lesions. There was no treatment which, by the wildest stretch of the imagination, could be considered effective. The early history of the disease was collected by Ricci (20, 21), to whom we are indebted for part of the following.

Among the confused ideas extant at the end of the eighteenth century, the accurate description written by Matthew Baillie in 1793 is refreshing. "This disease (malignant ulcer of the cervix) is certainly as formidable as cancer, because it terminates fatally, but its progress is different from that of cancer in other parts of the body. There is no enlargement of the uterus; ulceration continues until a great part of the uterus is destroyed. The disease begins in the cervix, and when it has made a great progress, the contiguous parts, as the rectum and the urinary bladder, are often involved in it." Terms such as "scirrhus enlargement," "fleshy tubercles of the uterus," and "malignant ulcer of the

cervix" were in common use. The name "carcinoma uteri" was introduced in 1821, and a decade or so later "cancer" became the accepted designation.

As early as 1850 Rokitansky stated that cancer was more frequently seen in the uterus than in any other organ of the human body. About the same time Scanzoni believed that frequent childbirth and obstetric injuries of the lower part of the uterus influenced the development of cervical cancer. He noticed that it was more common among city than among rural women, and thus felt that the manner of living influenced its origin. On the other hand, Scanzoni shared the prevailing opinion of the times that the most important etiologic factor was emotional, including grief, worry and sorrow.

During the first trimester of the nineteenth century treatment included blood letting, cupping of the lower abdomen, application of leeches to the cervix, starvation of the patient to prevent nourishment of the diseased organ, rest to prevent "stagnation" of the uterus, evacuants to deplete the blood, mustard and pitch plasters to the abdomen, vaginal irrigations and internal administrations of drugs. Also, during this period, cautery by a hot iron and by caustic chemicals was in vogue. Later, and until the end of the nineteenth century, gold chloride, zinc chloride, concentrated nitric acid, and carbolic acid were employed as chemical cauterizing agents.

History of the Operative Attack. Lack of success from the use of local applications led to attempts toward the end of the eighteenth century at surgical removal of the cervix. Obviously, amputation was the first procedure to be tried. By 1810 the Academy of Medicine at Vienna offered a prize for the best dissertation on the indications, limitations and most satisfactory method of procedure. Cervical amputation as a method of treatment of cancer was as useless then as it is today. Charles D. Meigs, the Philadelphia obstetrician who opposed the introduction of chloroform and bitterly fought Oliver Wendell Holmes' ideas on the contagiousness of puerperal fever, happened to be right concerning his stand on cervical amputation for the treatment of carcinoma. In a lecture to his class during the academic year of 1846-1847 he said, "I think the remark made to me by an eminent Philadelphia surgeon sometime since, is worthy of being repeated: 'If the cervix was cut off and the woman recovered, it affords the most uncontestable proof that the operation was unnecessary'."

Vaginal hysterectomy as a treatment for cervical carcinoma was also attempted. The first deliberate attack was made in 1813, and by 1856, 25 authenticated cases of vaginal hysterectomy for this cause were summarized. Only 3 women survived. Ricci believes that in the light of our present knowledge it is doubtful if cervical cancer was present in all instances. Some of these early attempts at cure by vaginal operation read more like descriptions of the scenes in a slaughter house rather than those of an operating theater, with the exception that the woman usually did not die until near the end of the operation. Hysterectomy for cervical carcinoma, by either the vaginal or the abdominal route, fell into disrepute until the dawn of the Listerian era of modern surgery.

In 1848, Dieffenbach called the operation murderous, and as late as 1875 Scanzoni said that it belonged to history and should never be performed.

In passing, it might be noted that the first successful abdominal hysterectomy with survival of the patient was accidentally performed in 1853 in Lowell, Massachusetts, by Walter Burnham (4). He opened the abdomen to remove an ovarian cyst and found instead a myomatous uterus. The patient vomited, the tumor mass was extruded from the abdomen and could not be replaced. Burnham, therefore, was forced to perform hysterectomy. Three months later, in the same city, Gilman Kimball (8) deliberately performed abdominal removal of the uterus after premeditation, rather than as an accidental procedure. Since the patient survived, the credit for the first successful performance of hysterectomy belongs to him. Storer (31), the fourth man successfully to perform hysterectomy in America, gives an excellent summary of the history of the operation. However, the problem was not solved, because both Burnham and Kimball were frequently unsuccessful in subsequent attempts and each came to believe the operation to be a formidable procedure.

Even after anesthesia, antisepsis and hemostasis brought the mortality rates of hysterectomy out of the zone of prohibitive risk, it was recognized that the operative attack on carcinoma of the cervix must include more than hysterectomy. Pawlik (19) advised extensive dissection of the parametrial tissue in 1890, and introduced catheters to identify the ureters.

Mackenrodt (11) suggested a method for wide parametrial dissection in 1894. In this country, J. G. Clark (6), during the time he was resident gynecologist at the Johns Hopkins Hospital, devised an operation to include removal of the regional lymph nodes. Emil Ries (22) of Chicago independently conceived and executed the same procedure.

Wertheim (35) in 1900 published his paper on the abdominal removal of the cancerous uterus with wide dissection of the surrounding tissues, and the operation he described became the accepted standard for all who attempt the surgical removal of cervical cancer. Briefly, it begins with total hysterectomy and bilateral salpingo-oophorectomy, and includes wide dissection and removal of the parametrial and paravaginal tissues together with the upper half of the vagina. To do this requires visualization, dissection and lateral retraction of the ureters. In addition, the operation often includes bilateral removal of the obturator, hypogastric and iliac lymph nodes, in other words, iliac lymphadenectomy. When it was first performed by Wertheim, the mortality rates varied between 15 and 25 per cent. Bonney (3), in 1935, reported that he was able to reduce his operative mortality rate among a series of 483 personally performed Wertheim operations from 20 per cent in the first 100 patients to 9.5 per cent in the last 200. In this country, Lynch of the University of California was the chief, and for many years the only prominent, advocate of radical operation for cervical carcinoma.

Prior to Wertheim's contribution, Schauta (24) devised a radical operative procedure, performed by the vaginal route. Obviously, lymph gland dissection

was impossible. Otherwise the operation was equally as radical as Wertheim's. Schauta's operation did not find favorable reception in America.

HISTORY OF IRRADIATION

Radium. Curie discovered radium in 1898 and treatment to exposed body surfaces began almost at once. O'Brien (14) states that Becquerel accidentally burned himself in 1901 when he left a tube containing a radium salt in his vest pocket for some little time. It is of great interest that the first suggestion to employ radium interstitially, or bury it in the diseased tissues, came in 1903 from Alexander Graham Bell, the inventor of the telephone. The first authenticated use of radium for the treatment of cancer of the cervix was by Margaret Cleaves in 1903. Others, including William James Morton, Truman Abbe and W. H. A. Dieffenbach, quickly tried the new medium, but Robert Abbe was the first to report survival of a patient for a period of 8 years. The principle of filtration, upon which all modern radium therapy is based, was announced in 1907 by H. Dominici.

By 1915 Howard Kelly and Curtis Burnam of Baltimore reported a series of 213 patients treated during the preceding 6 years. Henry Schmitz of Chicago treated 112 women by radium for cervical carcinoma prior to 1915.

Between the years 1918 and 1925, dosages and filtrations became more or less standardized. This is not to say that there has been no advance in radium technic since that time.

Roentgen Therapy. A concise summary of the early use of Roentgen rays in the treatment of carcinoma of the cervix is given by Behney (2). "Soon after Roentgen rays had been discovered and their therapeutic value was appreciated, they were utilized in the treatment of carcinoma of the cervix. At that time the only X-ray therapy available consisted of rays of long wave-lengths, the so-called "soft rays." These were applied to the abdomen externally, and accomplished little more than to burn the skin. The depth dosage obtainable with these long wave-length rays was so insignificant that it had no appreciable effect on the carcinoma. In 1902, E. W. Caldwell suggested irradiation of lesions on the cervix with these long wave-length rays by moving the X-ray tube close to the vulva and, with various types of specula, to expose the lesion on the cervix to the rays. This method proved more successful than irradiation through the abdominal wall, but here also the effects were superficial and palliative for only a short period of time.

"The introduction of radium for the treatment of this disease proved so much more satisfactory that for a time X-ray therapy was abandoned in the treatment of carcinoma of the cervix. In the comparatively few instances in which X-rays were employed, they were given more as a placebo, in hopeless cases, than with the expectation of accomplishing anything truly beneficial to the patient's lesion. Later when X-ray equipment of higher voltage, emitting rays of shorter wave-length (so-called "hard rays"), became available, roentgenologists applied these to hopeless cases of carcinoma of the cervix as well as in other diseases. Reports of good palliative results in the later stages of carcinoma of the cervix were

received from far and wide, yet because of previous disappointments with the use of long wave-length X-rays, gynecologists and surgeons were slow to accept this type of therapy in the treatment of cervical cancer."

Between the years 1930 and 1935, irradiation by combinations of radium and X-ray reached a high stage of development, and 5-year survival rates at first equalled, and in early cases surpassed those obtained by operation. It was recognized that irradiation was not without its dangers, and superficial tissue necrosis was encountered frequently in the early days. Later, as depth doses were increased, proctitis and enteritis took an appreciable toll of life. For a time diminution of the blood supply of the upper portion of the femur resulted in numbers of pathologic fractures, until the use of the lateral ports for deep therapy was abandoned. Although these complications could be prevented or minimized, the woman undergoing extensive deep X-ray treatment always experienced weeks and often months of anorexia, nausea and sometimes vomiting.

By and large the results were satisfactory and the dangers surmountable, so that most of the medical profession felt the problem of treatment of carcinoma of the cervix was standardized, until such a time as the cause and cure of cancer were discovered. Consequently, most of the workers in the field turned their attention toward efforts at prophylaxis, improvement of existing technics and education of the public. A few hardy souls, like Victor Bonney in England and Frank W. Lynch in America, continued to perform Wertheim's operation, but by and large it was abandoned. There were 3 main reasons for this: (1) radiation technics offered excellent hope of 5-year arrest to those women appearing for treatment during the early stages of the disease, (2) the primary operative mortality rates were high in the hands of seasoned and expert operators and prohibitive in the hands of others, (3) there was an insufficient number of gynecologists trained to perform the operation, one of the most difficult in the entire field of surgery. As a corollary to this last, it may be stated that the operation is also severe on the operator. Not only are knowledge and skill prerequisite, but in addition considerable physical stamina and emotional stability are demanded of the man who performs it. It may truly be classified as a "character building" operation.

REFINEMENTS OF EXISTING METHODS

Classification. Impetus toward improvement of existing facilities stemmed from the observation by Henry Schmitz (26) of Chicago in 1927, that treatment was effective in inverse ratio to the objectively observed, anatomic spread of the cancer at the time the patient presented herself. Later, the League of Nations offered an alternate clinical classification, differing only in details from that of Schmitz. The value of these clinical classifications for prognosis, evaluation and comparison of the effects of treatment has been enormous.

Prophylaxis. The early recognition that childbirth, in some way, favored the development of cervical carcinoma led to many false inferences and some sound clinical investigation. By the early part of the 20th century, many felt the disease appeared only in women experiencing an obstetric episode. Conversely,

it was argued by some that the nullipara escaped. These over-enthusiastic inferences were gradually supplanted by the saner view that long continued, chronic cervical inflammation was a definite etiologic factor in the causation of cervical cancer. Two names deserve mention in this connection. In 1941, Cashman (5) of Pittsburgh reported that 10,000 patients with chronic cervicitis were treated with deep cauterization, and in 1945 stated that "only 2 cases of cancer of the cervix are known to have occurred in this series." Catherine MacFarlane, Sturgis and Fetterman (9, 10) of the Woman's Medical College of Philadelphia, undertook to follow more than 1000 volunteers over a period of years in order to ascertain the effect of cervical disease upon the etiology of carcinoma of the cervix. To date they have made 2 reports confirming the significance of cervical infection and erosion.

Irradiation. Space does not permit an attempt to detail, or even mention, the number and variety of improvements in the technical aspects of both radium and x-ray therapy. In general, it is well recognized that radium, applied intravaginally or within the cavity of the uterus, cannot possibly deliver a cancericidal dose to cells as far away as lymph nodes of the lateral pelvic wall. Therefore, practically all radiologists employ both X-ray and radium in treatment.

Ancillary Operations. This fact led Taussig (32, 33) to begin, in 1930, revival of that part only of the Wertheim operation involving dissection of the regional lymph nodes. Taussig did not remove the uterus, and relied upon irradiation for basic treatment. Whatever else this operation did, it broadened our knowledge concerning the incidence of lymph node involvement in early cases of cervical cancer.

Another operation sometimes employed as ancillary treatment is ligation and division of one ovarian and both hypogastric arteries. It is useful to stop otherwise intractable hemorrhage in the terminal stages of the disease, and sometimes in patients with deeply eroded, but curable, lesions. These 3 vessels may be ligated and divided without producing necrosis of any part of the body supplied by the hypogastric or ovarian arteries.

Lay Education. The American Cancer Society instituted, during the 1930's, intensive campaigns to educate our people, since it is well recognized that more than 90 per cent of all women with carcinoma of the cervix could be cured by *existing methods* under ideal circumstances. Contrast this with salvage rates of 20 to 30 per cent, variously reported from acceptable sources over the world. Such ideal circumstances presuppose that every woman experiencing vaginal spotting will seek and receive competent diagnostic authority within a few days after noticing the very first spot of blood. They also presuppose that adequate facilities for the treatment of all who apply will be available at a not too great distance from the place of residence.

Summary. The state of general knowledge concerning cancer of the cervix at about the year 1935 might be summarized as follows: The role of chronic cervicitis in etiology was understood. Excellent clinical classifications of the extent of the disease were available. Diagnosis was made by inspection, palpation, and ultimately biopsy. Extensive and effective irradiation treatment was

possible since the limits of tolerance were well known and the principles of filtration understood. Irradiation by both radium and x-ray was the generally accepted method of treatment, and most of us felt that we had gone about as far as we could reasonably hope, except for certain technical refinements. Therefore, the problem of early recognition of the symptoms of the disease by the patient herself, and the extension of existing facilities of treatment became increasingly important and efforts along these lines were intensified.

Such was the state of complacency reached by most gynecologists and radiologists in the years immediately preceding World War II. In the meantime, 3 separate lines of endeavor, destined to produce a tremendous impact upon the philosophies underlying diagnosis and treatment of cervical carcinoma, were quietly being pursued. These lines of endeavor were: (1) extension of knowledge concerning intraepithelial carcinoma or carcinoma in situ, (2) development of exfoliative cytologic methods and knowledge, and (3) revival of operative attack in the light of modern surgical advances.

INTRAEPIHELIAL CARCINOMA

In 1910, I. C. Rubin (23) of New York City published a paper on "The Pathological Diagnosis of Incipient Carcinoma of the Uterus," written while he was working in the Second Frauenklinik in Vienna under direction of Professor Schottländer, Chief of the Laboratory. The work was based on 3 patients. Rubin stated, "In the first place it is obvious that, histologically considered, the carcinoma must have a beginning. The reason why we cannot make an absolute diagnosis in the earliest stages of the growth is due to the fact that the material thus far has not been available." He gave us the criteria of carcinomatous epithelium:

1. An indistinct, uncertain definition of cell outline, particularly in the deeper layers (germinal, proliferating).

2. The presence of irregular, large, intensely stained nuclei, occasionally grouped in clumps.

3. No definite stratification, only partial parallelism of the basal cells (more often they are seen to be irregularly disposed, or at a slant toward the tunica propria).

4. The marked nuclear granulation. This sign deserves special attention because, according to Schottländer, it is very frequently seen in carcinoma which has not yet undergone cornification."

In the same paper he stated that, "The changes observed in the atypical cell proliferations constitute the most essential diagnostic signs of malignancy."

Two years later, Schottländer and Kermauner (28) published a monograph on the early diagnosis of uterine carcinoma, and noted cells extending over the surface similar to those in an underlying invasive lesion. Walter Schiller (25), in 1928, felt that a number of young carcinomas, because of their small size, escaped clinical examination. He found it useful to perform curettage of the surface epithelium with a spoon, and recommended this method in preference to excision of a piece of tissue. Despite these early pioneering efforts, beginning

almost 40 years ago, little attention was given to the histologic beginnings of cervical carcinoma until Schiller began writing extensively on the subject in 1933. In this country, Smith and Pemberton (29), and Schmitz and Benjamin (27), were among the early writers on the subject, which received great impetus by the publication in 1944 of an article by TeLinde and Galvin (34). In a recent article (7) they conclude, "From these studies it would thus appear that carcinoma in situ or intraepithelial carcinoma should be considered strictly as a histologic diagnosis and be regarded as indicating one of 3 clinical possibilities:

1. That the biopsy has been taken from the periphery of an advanced cervical cancer as was originally described by Schottländer and Kermauner.

2. That microscopic invasive cancer is present elsewhere in the cervix as was the case in 55 of our 75 cases.

3. That only carcinoma in situ is present and no invasion has as yet taken place. This was found to be the case in 20 of the 75 cases which we studied."

They point out that, "the average age of our 75 women with cancer in situ was 37.1 years,—in contrast to the average of 48 of women with clinical gross cervical cancer."

In order to find these patients, TeLinde and Galvin laboriously performed thousands of routine cervical biopsies.

In summary, it may be said that, histologically considered, carcinoma must have a beginning. In the beginning, the histologic changes relate to anaplasia of the cells of the deeper layers of the cervical epithelium and probably do not include actual invasion outside this layer. The anaplastic cells may seem, at first inspection, to be located entirely within the epithelium, intraepithelial carcinoma, or carcinoma in situ. However, as TeLinde and Galvin showed, further search of additional sections will frequently reveal an area of frank invasion. Clinically, carcinoma of the cervix must exist in a dormant state for years before beginning the career of invasion leading to manifestations of the disease we have known in the past. In other words, the phase of clinical manifestations of cervical carcinoma is of relatively short duration as contrasted with the preclinical phase. The preclinical is perhaps divisible into 2 parts: (1) actual invasive carcinoma which has not yet produced surface ulceration, and (2) nests of anaplastic epithelial cells confined entirely, so far as observable after extensive search of many tissue sections, to the cervical epithelium. Whether or not these 2 parts of the preclinical phase are identical must be decided in the future.

EXFOLIATIVE CYTOLOGY

The second line of 3 endeavors, destined to upset most of our formalized concepts of cervical carcinoma, was the recognition that cancer cells, as well as normal vaginal cells, exfoliate and may be recovered by the vaginal smear to be recognized by appropriate staining technics. The genesis of the idea dates back 32 years to an historic landmark in the field of female endocrinology. In September, 1917, Stockard and Papanicolaou (30) published the results of their studies on the physiological cycle of the vaginal epithelium of the guinea pig, and gave to scientists for the first time a method of identification of the female

sex hormone. The importance of this paper can hardly be overestimated, since the new method unlocked the door to research on the endocrinology of reproduction. By 1928, Papanicolaou (15) recognized the occasional presence of atypical cells in the vaginal smear, and by 1933 established the existence of "The sexual cycle in the human female as revealed by vaginal smears (16)." In 1941, Papanicolaou and Traut (17) presented a paper on the "Diagnostic value of vaginal smears in carcinoma of the uterus." Even so, the idea did not begin to gain momentum until these men, Papanicolaou, the anatomist, and Traut, the gynecologist and pathologist, published their monograph entitled the "Diagnosis of uterine cancer by the vaginal smear (18.)"

The principle is very simple. Epithelial surfaces, wherever situated, constantly shed cells. If the epithelium is normal, the exfoliated cells are normal. If the epithelium is malignant and anaplastic, cancer cells are shed and may be recognized by appropriate staining technics. Theoretically, the method is applicable to any body surface, cavity or secretion from which exfoliated cells may be recovered. These include lung, stomach, vagina, rectum, urinary tract, pulmonary and ascitic fluid. Practically, the study of exfoliated cells as a method of cancer detection is useful for uterine, bronchial and urinary tract lesions. In the latter 2 instances, usefulness is largely dependent upon the fact that simple methods of detection are otherwise unavailable.

Exfoliative cytologic methods evolved from research in the field of reproduction and are most applicable to detection of carcinoma of the uterine cervix. It is, therefore, quite understandable that the gynecologist not only has a stake in the method from the historical standpoint, but also is vitally concerned with the tremendous practical benefits offered by study of the exfoliated cells of the epithelia of the reproductive tract of patients whom he sees in daily practice.

Two methods of recovery of cells exfoliated from vaginal epithelium are generally employed: (1) aspiration with a pipette of the small amount of fluid omnipresent in the cervical canal and upper vagina, and (2) mechanical scraping of the entire circumference of the cervical surface at the junction of the squamous and columnar epithelia. This may be done with a wooden spatula, as recommended by Ayre (1), or with a metal spoon as suggested by Schiller (25) in 1928. Schiller, however, did not scrape the entire circumference, limiting this to areas exhibiting a positive iodine test. It is important to clarify the difference between these 2 methods. The first is definitely recovery of only a few exfoliated cancer cells, which may be fresh or degenerated and, therefore, difficult to recognize. The second is a deliberate removal of tissue, and may be classified as a biopsy. In effect, scraping is a *surface biopsy*, and is highly desirable because it overlooks no part of the squamo-columnar junction, recognized as the usual site of origin of cervical carcinoma. It is painless, may be done without anesthesia by a properly trained technician, and does not necessitate hospital residence. Since the surface biopsy removes cells down to the basal layer and surveys all parts of the squamo-columnar junction, it will frequently detect carcinoma missed by depth biopsy. The latter must be directed at a specific place in the circumference of the cervix, and thus, may fail to demonstrate an existing lesion. This point was thoroughly demonstrated by a recent

patient whose cervical scrapings contained anaplastic cells. Since 4 slides, 1 for each cervical quadrant, were made, it was known that the anaplastic cells appeared in profusion at a point of the circumference designated as 3 o'clock. A cone-shaped piece of tissue, containing the entire squamo-columnar junction and most of the gland bearing area of the endocervix, was removed with the patient under anesthesia. Although attention was concentrated at the 3 o'clock area, it was not until the 30th tissue section was cut from this region that carcinoma *in situ* was found. This case record will be published later in detail.

Exfoliative cytologic methods, including surface biopsy applied to study of the uterine cervix, are no longer in the experimental category. There is no doubt that competent physicians, trained in the technic, can recognize cancer cells with a percentage of error which decreases as skill and experience increase. There need be no controversy over the relative merits of depth biopsy and cytology and each method should supplement the other. Deep tissue biopsy reigns supreme for confirmation of the diagnosis of clinically demonstrable lesions, and must remain the final arbiter in all cases, at least for some time to come. On the other hand, cytologic methods, especially surface scraping, *for the first time offer a simple and dependable test for the detection of carcinoma in its preclinical phase.* Prior to the advent of exfoliative cytology, preclinical carcinoma and carcinoma *in situ* were discovered either by accident or by laborious multiple and painful biopsies. In other words, cytology represents a simple, effective and painless approach to the study of the preclinical phase of cervical cancer. *This is the tremendous benefit of the method.* We are now able to penetrate, with relative ease, the diagnostic mysteries surrounding carcinoma of the cervix before it starts the clinical career which, unchecked, results in rapid destruction of the host. Again and again we are startled from complacency by finding anaplastic cells in surface biopsies of women with no visible cervical lesion. Tissue biopsy, usually a cone shaped piece of tissue containing the entire circumference of the squamo-columnar junction, confirms the diagnosis. In other words, we have once again found cervical cancer in a woman presenting not the slightest sign or symptom of the disease. *In the past many gynecologists, including myself, were quite proud of our ability to diagnose all cases of carcinoma of the cervix by sight and touch. Just why we thought we possessed a "microscopic eye," I do not know, but that was the fact.* Even today, there are those who continue to believe in their clinical abilities and doubt the existence of pre-clinical cervical carcinoma. Certainly, the smallest possible carcinoma visible to the naked eye does not just suddenly appear as an ulceration from nowhere, but must have an origin. The method may be employed, not only to detect, but also to follow the course of preclinical cancer. Finally, it provides a most convenient method of following the course of patients treated by irradiation, and thus detecting recurrence at the earliest possible moment.

What of the future of exfoliative and surface cytology? At the present there is an insufficient number of trained physicians, and the cost is too great, to permit mass surveys of the population except on the basis of clinical experiment. On the other hand, there is evidence to show that when surveys are made with intelligent selection of patients, the incidence of the number of cases found rises

appreciably. So employed, the possibility that cytologic methods will become part of our office diagnostic routines, is not too remote. If every woman over 35 years of age, especially if she presents cervicitis or erosion, could have the benefit of cytologic study whenever she visits a doctor for any reason, most cervical cancers would be cured by existing methods. As a matter of fact, we found preclinical cancer, subsequently proved by biopsy, once in every 40 such women. This incidence dropped to 1 in 174 when patients were tested routinely, without thought of selection.

Among more than 2700 women admitted to Parkland Hospital and studied by means of the vaginal smear, 20 patients with no clinical evidence of cervical carcinoma were subsequently shown by tissue biopsy to have preclinical cancer. Tissue biopsy has always been performed after anaplastic cells were found in the vaginal smear, and in no instance has any form of treatment been predicated solely upon cytologic study. Details of our experiences have been, and will be published elsewhere, and need not be given here. It may, however, be in order to say that our experiences closely parallel those of others employing the method.

REVIVAL OF THE OPERATIVE ATTACK

Meigs (12), in 1944, reported no primary operative fatality in a series of 47 patients submitted to Wertheim's operation. He deliberately chose to reopen the question of operative attack for a number of reasons, summarized as follows: "(1) If the cervix has been removed, there is no chance for a recurrence in it. (2) If the cervix has been removed, no cervical cancer can regrow in it as a recurrence. (3) Certain cancers of the cervix are radiation resistant (4) There will be less damage to the bowel if surgery is undertaken (5) From the work of both Bonney and Taussig it is obvious that patients with lymph node metastases can be cured by surgery in some instances," Meigs does not believe it is possible to cure with radiation cancer in lymph nodes deep in the pelvis. In a later article (13) Meigs reported a grand total of 65 women operated on without primary fatality. Eight of them suffered ureteral fistula, which according to him is, "The only really serious and annoying complication." He believes that this complication will be minimized in the future. "Lymph nodes were involved in 12 patients: the iliac nodes in 6, the obturator nodes in 7 and the ureteral nodes in 1. More than one area was involved in 2 patients. Therefore, 18.4 per cent of these very early cases had lymph node extension"

Meigs contributed to the operative history of cervical carcinoma by re-evaluating the mortality risk in terms of modern care, since one of the greatest objections to the Wertheim operation was the excessive death rate. On the other hand, we must remember that these operative mortality rates were assessed at a day and time when modern pre- and postoperative care was unavailable. All of us recognize that adequate hemoglobin values, red blood cell count, fluids, antibiotics, early ambulation and a speedy return to normal function have strikingly reduced operative mortality rates in all fields. It was, therefore, reasonable to assume they would serve a similar purpose for the radical operation for carcinoma of the cervix. Since Meigs' contribution, others are also endeavoring to decide the place of the Wertheim operation in the treatment of cervical

patient whose cervical scrapings contained anaplastic cells. Since 4 slides, 1 for each cervical quadrant, were made, it was known that the anaplastic cells appeared in profusion at a point of the circumference designated as 3 o'clock. A cone-shaped piece of tissue, containing the entire squamo-columnar junction and most of the gland bearing area of the endocervix, was removed with the patient under anesthesia. Although attention was concentrated at the 3 o'clock area, it was not until the 30th tissue section was cut from this region that carcinoma in situ was found. This case record will be published later in detail.

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cancer. We do not believe the answer to this question is available at the present time. On the other hand, and as a result of Meigs' demonstration, we may not today dismiss the operative attack on carcinoma of the cervix from consideration, and channel all therapeutic efforts toward irradiation.

THE FUTURE

It is exceedingly interesting that the methods of treatment of cervical carcinoma, standardized 10 years ago, are in a state of flux today. Ultimately, we hope for knowledge of the etiology of all types of malignant disease. Perhaps then, it will be possible to devise both a satisfactory test and a specific treatment. Until then, we must utilize all existing methods offering reasonable hope.

The comparatively recent introduction of cytologic methods now offers the possibility of detection of cervical carcinoma in its incipency. Existing evidence suggests that the duration of the incipient, preclinical, or asymptomatic phase of the disease is many times longer than that of the clinical phase. This suggests further that from the standpoint of cancer detection it would be unnecessary to make frequent studies on every woman, since the duration of the period of latency is a matter of years. Although mass surveys of the female population by means of cytologic methods is scarcely feasible at the present time, it may be that proper selection of patients will reduce the labor and cost of case finding to a reasonable level.

Operation, once the only hope of cure, was almost entirely supplanted during the 1920's and early 30's by irradiation, but now is being critically reviewed in an effort to determine its place. In our endeavors to decide this question, it is certain, as Meigs said, that selection of patients is important. Selection may be based upon the chance of cure, as well as upon technical feasibility. It is likely that operation will become the treatment of choice for incipient, pre-clinical carcinoma detected by cytologic methods, since it can be removed surgically with every possible hope of cure. Perhaps very radical operative attack may be reserved for radio-resistant carcinomas, which either continue to shed anaplastic cells, or begin again to do so, shortly after cessation of irradiation therapy.

In the light of the impact of knowledge recently acquired, who can speak with authority today to tell us how any patient with carcinoma of the cervix should be treated?

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num of equipment. The spermatozoa are easy to distinguish microscopically and are never present except under the hormonal stimulation described, so that theoretically the presence of one sperm means a positive test. In addition, results are available as soon as one hour after the injection and never longer than 3 hours. Stocks of male toads have been easy and cheap to obtain. They require no elaborate tanks or boxes and they live for weeks without food. Each animal may be used for several tests. The author concludes that in cases of pregnancy and in controls the favorable results of other workers are confirmed by this present series. 1 figure.

(The peregrinations of some of the newer developments in obstetrics occasionally carry one rather far afield. For instance, one of the most popular of modern tests for pregnancy, the Hogben or Zenopus test, is sometimes called the "frog test" and sometimes the "toad test;" and the question arises as to which is correct and what, after all, is the difference between a frog and a toad. I am sure I could not answer this stirring question were it not for Webster who comments as follows: a typical frog (genus *Rana*) differs externally from a typical toad (genus *Bufo*) in its more aquatic habits, smooth skin, webbed feet, greater agility in leaping and swimming, and in certain anatomical characters, but many intermediate forms occur which are called by either name. The typical toads are generally terrestrial in their habits, except during the breeding season, when they seek the water. They have a short, squat body, comparatively weak hind legs, and are covered with a rough warty skin in which are glands that secrete an acrid fluid irritating to the lips of an attacking animal. Webster refers to *Zenopus* as a genus of African aglossate toads.

Since the *Zenopus* has broadly webbed hind feet it is apparently an atypical toad, but toad it is according to Webster, and if the term "frog test" or "toad test" is to be applied to this procedure at all, the latter would seem to be more accurate. Actually, to be at all accurate these days in referring to these tests, it is necessary to be more specific and refer to the genus as well as the sex of the test animal. Thus, there is the popular female *Zenopus* test, or Hogben test, but there is also the possibility that the male *Zenopus* may be used for this purpose because it is said by Robbins, Parker and Bianco to be 10 times as sensitive to chorionic gonadotrophin as the female *Zenopus*. (Endocrinology 40: 227, 1947). The test reported in the above abstract is another toad test, a male toad test, but to be at all specific it would appear desirable to refer to it as the male *Bufo* test to differentiate it from the male *Zenopus* procedure as well as the Hogben test. All these, however, are "toad tests."

From a practical viewpoint, it is important to note that the male frog test, or *Rana pipiens* test, is gaining ground in this country because of its accuracy, economy, simplicity and rapidity. Especially appealing is the fact that this type of frog, the ordinary leopard frog, is indigenous to the United States and easily obtainable. The gratifying results secured with this test by 2 groups of investigators were discussed in an editorial note in the August, 1948 issue of the Survey, Page 462-463. We have ourselves used it in over 150 cases with much satisfaction.—Ed.)

Obstetrics

MANAGEMENT OF NORMAL PREGNANCY, LABOR AND PUERPERIUM

THE MALE TOAD TEST FOR PREGNANCY

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Lancet, 2: 923-926, (Dec. 11) 1948

Injection of urine into animals has been used for the past 20 years as a test for pregnancy. The author has used as his test animal the male toad of the species *Bufo arenarum* Hensel, indigenous to South America. In the male toad the liberation and expulsion of spermatozoa are controlled by the pars anterior of the hypophysis, and injection of pituitary gonadotrophins causes spermatogenesis. When chorionic gonadotrophins from pregnant urine are used, spermatogenesis is effected and the spermatozoa appear in the urine within a short time, usually in about 3 hours. In addition, spermatozoa never appear in the urine except in amplexus or under such experimental conditions.

The technique for this test is very simple and results are obtained within several hours. Fresh morning urine is collected and 10 ml. of this untreated urine is injected slowly beneath the skin. The toad is then placed in a separate well-ventilated dish containing enough water so that the toad may soak himself but not enough to cover him. At the end of 2 to 3 hours the toad is catheterized, using a bulbed pasteur pipette. A drop of the urine is examined microscopically and in the case of a positive test a large number of spermatozoa will be seen. After a rest period of 6 days the animal may be used again. Previous reports on this pregnancy test were summarized by Galli Mainini (1948) and in 2661 collected cases the accuracy ranged from 98 to 100 per cent. There were no false positive results.

In the author's series of 100 samples of pregnant urine, there were only 4 instances in which positive results were not obtained at 3 hours, and one of these cases became positive one hour later. The other false negatives were attributed to dilution of the urine or to the time during pregnancy at which the test was done. It was found to be less reliable in the second and third trimesters. In special circumstances such as abortions, threatened abortions, amenorrhea associated with uterine fibroids, etc., the test was found to be helpful and the results closely paralleled those of the Friedman test.

The advantages of this test are for the most part quite obvious. Its reliability is best indicated by the foregoing brief summary of previous results. The technique is simple and the complicated treating or modifying of the urine is avoided. The results of the test are definite and easily demonstrable with a mini-

THE INFLUENCE OF CIGARETTE SMOKING IN PREGNANCY

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Zentralbl. f. Gynäk. 70: 18-31, 1948

The amount of smoking during the war and the postwar period in Germany has increased greatly. Therefore, many influences of tobacco smoking have become plain.

One hundred grams of cigarette tobacco contain 2 grams of nicotine and nicotine bases. Nicotine affects the vegetative nervous system and the capillary circulation. It affects the former through the ganglia, which it at first stimulates and then depresses, hindering the propagation of impulses from preganglionic to postganglionic fibers. Accordingly, nicotine influences both the sympathetic and the parasympathetic systems.

Nicotine also causes capillary spasm. With prolonged injury, endarteritis and fibrosis of the walls of the arteries may occur. The capillary spasm caused by nicotine produces a slowing of peripheral blood flow and lowering of skin temperature.

Pregnancy per se produces very marked changes in the vegetative nervous system. Because of tobacco's action upon the same system these changes are greatly augmented.

Nutritional deficiency also contributes to the picture. In the Ruhr, pregnant women have been receiving less than 50 per cent of their protein requirements during the postwar period.

The author compared 112 pregnant smokers and 1381 pregnant non-smokers. Hyperemesis occurred in 62.5 per cent of the smokers and 21.4 per cent of the non-smokers. Ptyalism occurred in 16.1 per cent of the smokers and only 1 per cent of the non-smokers. Renal and ureteral pain, bladder colic and urinary frequency (without demonstrable pathologic findings in the urine) occurred in 26.8 per cent of the smokers and only 13.5 per cent of the non-smokers. Biliary symptoms, such as upper quadrant pain and biliary colic, occurred in 21.4 per cent of the smokers and 14.5 per cent of the non-smokers. Cardiac neurosis, including precordial pain and pain running down the left arm, occurred in 35.7 per cent of the smokers and only 10 per cent of the non-smokers.

In 458 smokers, Bernhard found a 22.5 per cent incidence of miscarriage. 5000 pregnant non-smokers showed only a 7.4 per cent incidence of miscarriage. In the smoking group there was an incidence of 3.1 per cent of premature labor, while the incidence of premature labor in the non-smokers was only 0.86 per cent. Bernhard explains this by saying that nicotine causes contraction of the smooth muscle of the genital organs.

Bernhard also feels that nicotine poisoning may lead to hormonal disturbances

THE EFFECT OF TOBACCO ON ESTRUS, PREGNANCY, FETAL
GROWTH AND LACTATION (A CRITICAL REVIEW
OF THE LITERATURE)

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North Carolina M. J., 9: 519-522, (Oct.) 1948

The authors have reviewed the extensive literature on the toxic effects of tobacco and have concluded that there remains a dearth of dependable data upon which definite opinions could be formed. The main discrepancies in the experimental work have been the failure to recognize the differences between animal and human subjects in such factors as: (1) the relative dose of nicotine; (2) the mode and rate of nicotine administration; (3) the matter of tolerance or habituation to nicotine; and (4) species differences in the response to nicotine.

Concerning the effect of nicotine on the estrus cycle, there have been conflicting experimental data. Large doses are apparently capable of stopping the estrus cycle in white mice and preventing pregnancy, but in doses comparable to the amount absorbed even by the heavy smoker, other investigators have failed to demonstrate any appreciable effect on the cycle in white mice. Clinical studies among women tobacco workers have shown a high incidence of delayed menarche, early menopause, menstrual disturbances, dysmenorrhea and endometritis. There is some experimental and clinical evidence which would indicate that women have a higher resistance to nicotine than men.

The effect of nicotine on pregnancy and fetal growth is also controversial. In the experimental animal an increased incidence of stillbirths and a decrease in body weight of the mother and offspring have been noted. However, the authors point out that the dose and mode of administration in animals differ greatly from that in the human, and the rate and amount of absorption have been overlooked. Chiasson found exceptionally high fertility and abundant lactation in a group of French women who were habitual pipe smokers. Among women tobacco workers, studies have shown that there are fewer pregnancies, more abortions and a higher infant mortality rate. There has been only inconclusive evidence to indicate that nicotine crosses the placenta.

Toxic doses of nicotine will suppress lactation for several hours to a day, but will not permanently impair lactation. Traces of nicotine have been found in the milk of women who smoked 20 to 25 cigarettes per day. No effect has been demonstrated in the nurslings of animals given large doses of nicotine, and the offspring on occasions show a resistance to the drug.

(See editorial note following next abstract.—Ed.)

THE INVESTIGATION AND TREATMENT OF "BORDER-LINE" CASES OF CONTRACTED PELVIS

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J. Obst. & Gynaec. Brit. Emp., 55: 401-417 (Aug.) 1948

The author has divided the investigation of cases of contracted pelvis into 6 phases; pelvic formation and capacity, size of fetal head, moldability of the fetal head, "give" in the maternal pelvis, degree of rigidity of the cervix and efficacy of the forces. The first factor can be determined with exactness by radiography, and the author advocates routine pelvic x-ray studies in all primigravidas. Minor variations in pelvic formation will be noted and the obstetrician will be prepared if difficulties arise. It has not been the author's experience that cesarean sections are more common when routine radiography is employed. The argument that such a procedure may "rattle" the patient does not seem valid. For routine purposes, a lateral view is best employed; however, if abnormalities are present a frontal view should also be taken. Some authors have suggested that the plane area is of more value in determining the pelvic capacity than measurement of the particular diameters. However, it must be remembered that the area which is determined radiologically may not always be the potential area if the malformation is irregular or asymmetrical. It would appear, however, that exact plotting of the areas at brim, cavity and outlet is of aid in sorting out the borderline cases and as the brim or outlet areas fall below 95-100 square centimeters, the frequency of dystocia increases.

Estimation of the size of the fetal head and of its adaptability to the maternal pelvis raises a particular problem in the "borderline" cases. Bimanual examination at the 36th to 37th week will usually exclude all except the "borderline" cases. Certain estimations as to the size of the fetus can be made on the basis of the size of the head and this will often influence the course of treatment followed. Radiographic cephalometry, though not always completely accurate, is of value in the questionable cases. Hope for further refinement of this procedure should increase its value in the future.

In estimating the degree of molding of the fetal head, consideration must be given to the size of the fetus, size and shape of its head and the attitude the head develops. The author feels that he can make fairly correct allowances for molding in cases of flat pelvis if the head assumes an anterior parietal position. It is commonly assumed that 2 to 3 mm. in one diameter is the molding which can be reckoned on; however, more may be expected if the head is poorly ossified, and less if the head is large and round, for then there is usually more ossification. Intrapartum radiography is recommended when trial labor does not progress as expected.

"Give" in the maternal pelvis results from softening of the ileo-sacral joints and symphysis pubis and pressure of the fetal head on the pelvic wall. The usual

and prolongation of pregnancy, with subsequent death of the fetus in utero. He states that in 118 smokers 5.1 per cent had stillbirths, whereas in 1352 non-smokers only 2.3 per cent had stillbirths.

Of the author's smoking pregnant patients 16.1 per cent had difficult labors whereas only 8.7 per cent of his non-smoking pregnant patients had difficult labors. This is attributed by the author to paralysis by nicotine of the sympathetic ganglia governing uterine contractility.

The author also states that higher incidence of puerperal bleeding, subinvolution and disturbances of lactation occurred in smokers than in non-smokers. These are attributed to disturbances of the autonomic nervous system.

Damage to the child, both through nicotine (which according to this author passes through the placenta) and through the mother's milk, is also cited as evidence of the evil effect of nicotine in pregnancy. It is further stated that children living in close quarters with mothers who smoke frequently suffer chronic nicotine poisoning which may eventually be fatal. The author states that in 249 cases he had 5 neonatal deaths which he believed were due to nicotine poisoning.

(Every year a number of letters reach my desk inquiring as to whether or not cigarette smoking is harmful in pregnancy; and in view of the widespread interest in the subject I am surprised that no American investigation of the question is available. Indeed, as Mengert has pointed out, there is an appalling dearth of knowledge on this subject. The role of nicotine in causing capillary spasm is well established. That the smoking of tobacco produces definite vasoconstriction in the majority of persons has been shown by studies of the skin temperature before and after smoking by Maddock and his associates (*Proc. Soc. Exper. Biol. & Med.* 29: 487, 1932; *Am. Heart J.* 12: 46, 1936), by Wright and Moffat (*J. A. M. A.* 103: 318, 1934) and by Barker (*Proc. Staff Meet. Mayo Clinic* 8: 284, 1933). The second group of investigators also demonstrated slowing and even cessation of blood flow through the capillaries during and shortly after smoking. It is agreed that these are effects which are due to nicotine, a known physiologic vasoconstrictor. If tobacco can affect the skin capillaries in this manner, there is every reason to suspect on theoretical grounds that it may act similarly on the spiral arteries of the uterus with deleterious effects on the products of conception as the result.

The above article by Bernhard is a severe condemnation of cigarette smoking in pregnancy and his findings would seem to bear out the theoretical objections mentioned above. But surely cigarette smoking cannot be as harmful to gravidæ as all this would indicate because, if so, the results of pregnancies in American women, in whom the practice is widespread, would not be as good as they are. However, as indicated, actual statistics are not available. Data on this matter would be very easy to accumulate and it is hoped that this provocative article will call them forth.—Ed.)

labor, may be submitted to premature induction. In carefully selected cases, symphysiotomy may be used with beneficial results. The deformity in the cases in which this procedure is used should be pretty well confined to the transverse diameter, for as much as 2 cm. may be added to this diameter, with the attending changes in the whole pelvic architecture.

(The author of this paper, Dr. J. M. Munro Kerr, was for many years Professor of Obstetrics and Gynecology at Glasgow University and is one of the preeminent figures in our specialty. In 1926 he was a guest of honor at the American Gynecological Society meeting and, in a memorable address, drew attention to the several advantages of the transverse uterine incision in low cervical section; and ever since, this type of operation has been known by his name.

The present paper reflects the author's rich background in the management of labor in the presence of pelvic contraction and is an astute and concise summation of the problem. It will be noted that this senior obstetrician, most of whose experience antedated the time of x-ray pelvimetry, advocates this procedure as a routine in all primigravidae. Another point to be observed is the emphasis he places on the cervix as a prognostic sign. Still another is the statement that good forces can very easily be killed by wrong or wrongly-timed sedatives or analgesics,—a warning that needs continual reemphasis. Finally, the next to the last paragraph of the abstract is as sane a directive on trial labor as I have seen.—Ed.)

ESTIMATION OF PELVIC CAPACITY

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J. A. M. A., 138: 169-174 (Sept. 18) 1948

The 5 components of cephalopelvic disproportion are: (1) size and shape of the bony pelvis, (2) size of the fetal head, (3) moldability of the head, (4) force exerted by the uterus and (5) presentation and position. Of these, only the first is susceptible to accurate measurement. Next to pelvic size, perhaps the most important component affecting the outcome of labor is the driving force of the uterus.

The present study, the purpose of which is to consider evaluation of the obstetric capacity of the entire bony pelvis, is based on a series of 935 patients measured radiographically and of whom 592 have been delivered. The 3 planes were portrayed graphically and a prediction of the outcome of labor made. Patients were allowed to progress to second stage pains with the membranes ruptured. A few were delivered electively by the abdominal route.

The author points out that the method of pelvic measurement is unimportant; the problems confronting the obstetrician are those of interpretation of measurements and evaluation of capacity.

From this study, it was observed that the best index of either inlet or midplane capacity is the product of the transverse and the anteroposterior diameters. A

give is about 2 mm. at each of these joints but it may be much more than this at the symphysis. The question of whether this "give" is present at the 36th to 37th week raises the problem of whether it is wise to induce labor at that stage of gestation. Often the "give" which occurs at labor will make a case which promised definite dystocia much less difficult than had been anticipated.

The condition of the cervix early in labor may also influence the course of treatment which is followed. If the obstetrician finds that the rigidity of the ring promises an unusually slow dilatation, it is generally inadvisable to push trial labor very far.

Generally speaking, the strength of the forces of labor is unpredictable. However, in certain instances, such as in the presence of the dystrophia dystocia syndrome or in the hysteroneurotic type of patient, one can surmise that the forces will prove ineffective. It must also be remembered that good forces can very easily be killed by wrong or wrongly-timed sedatives or analgesics. Moral support to the inexperienced patient may also give her confidence in her ability to effect delivery, a factor which plays a role in developing effective uterine forces.

In considering the treatment of the "borderline" cases of contracted pelvis, the author has recalled the history of the use of axis traction forceps, but he concludes that such operations have absolutely no place in the present-day methods of treatment. He also opposes the induction of premature labor in the primigravida, but feels that judiciously employed it fills a useful role in the management of the multigravida. However, he points out that even in the latter case, it is not without its dangers.

The trial labor usually enables one to foretell accurately whether or not a spontaneous outcome will result. A fair trial, however, in many instances cannot take place until after the membranes have ruptured and the fetal head has become adjusted to the pelvic brim, as often labor will be hesitant in the first few hours. The experienced obstetrician, nevertheless, can often surmise the probable course of events before the rupture of the membranes. After labor has proceeded 2 to 4 to 6 hours subsequent to rupture of the membranes, one can nearly always forecast the outcome by the position and attitude the head is assuming, the extent to which it is sinking into the pelvis, the quality and duration of the uterine contractions, the fortitude of the patient and the behavior of the fetal heart. In several large series of cases of spontaneous delivery in contracted pelvises, the fetal mortality is extraordinarily low. However, if the trial progresses more than 30 hours, the fetal mortality rises to appalling heights. The duration of the trial of labor that should be permitted will depend entirely on evaluation of each individual case.

The recent advent of antibiotics plus improved operative techniques has made cesarean section the procedure of choice if doubt exists in these cases. The lower segment approach with a transverse incision has been so perfected that a maternal mortality is a rarity. The author stresses the desirability of making the transverse incision as low as possible, for the scar in this area is often appreciably stronger. This is of special importance in the borderline case which, in the next

employment of radiographic methods. They should be employed in the presence of any one of the following observations:

- A. History
 - 1. Difficult labor, especially midforceps delivery
 - 2. Unexplained stillbirth
- B. Palpation
 - 1. Prominent ischial spines
 - 2. Sacral deformity
- C. Manual mensuration
 - 1. Inlet
 - (a) Ability to touch sacral promontory on vaginal examination
 - (b) External measurements below average
 - 2. Outlet
 - (a) Bisischial 8.5 cm. or less
 - (b) Sum of bisischial and posterior sagittal 15.0 cm. or less
- D. Nonengagement of fetal head at term in a primigravida.

(It is sometimes alleged that the use of x-ray pelvimetry increases the incidence of cesarean section. In the above paper, Mengert, who is one of our leading protagonists of x-ray pelvimetry, reports for his entire service an incidence of abdominal delivery of only 0.55 per cent,—about the lowest figure I have seen. The first paragraph of the above abstract makes plain the fact that there are some 5 factors which may be responsible for mechanical dystocia, of which only one is susceptible to x-ray evaluation. If the sole criterion for abdominal delivery is this one factor as determined by the roentgenologists' measurements, the number of unnecessary sections will of course soar, but if x-ray pelvimetry is used simply as an adjunct together with the other factors and if the whole ensemble is evaluated by a competent obstetrician, pelvic roentgenology will reduce, rather than increase, the incidence of cesarean section for mechanical dystocia.—Ed.)

EVALUATION OF RADIOGRAPHIC PELVIMETRIC TECHNICS

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M. Clinics North America 32: 1659-1671, (November) 1948

Soon after the discovery of the roentgen ray, an attempt was made to use it as a means of examining the pregnant abdomen and pelvis. Pelvimetry and the various methods of measurements resulted. The purpose of such measurements has been to correct for magnified distortion so that internal measurements could be made.

The clinician must be cognizant of the possible dangers of exposure to x-ray of the mother and fetus. No harm is done when accurate measurements of the x-ray dosage are made, when they are not repeated too often and when they are limited to the last trimester.

norm can be established for each plane and its capacity expressed in percentage of normal. Thus, it is possible to compare not only one pelvis with another, but also two planes of the same subject. In general, inlet and midpelvis tended to vary together. In other words, association of a large inlet and a small midplane, or vice versa, was relatively uncommon. There were, of course, glaring exceptions to this rule.

The average values of the diameters measured in 935 patients conform closely to accepted standards published by Stander (1945). After the inlet and midplane products were obtained, the central tendency of each was calculated. For the inlet it was: average 145, median 146 and mode 143. For the midplane it was: average 124.9, median 126 and mode 121. The average values were utilized and 145 was accepted as normal for the inlet and 125 as normal for the midplane. These figures represent 100 per cent for each plane, respectively, and capacity is expressed in percentage in relation to them. By a process of trial and error, it became obvious that 85 per cent of normal capacity of either inlet or midplane represented the border line between adequacy and contraction.

Concerning the outlet, there can be no serious outlet contraction without commensurate contraction of the midplane. Much of what, in the past, we have termed outlet contraction actually is midplane contraction. During the last few months the progress of obstructed labor has been checked with lateral roentgenograms. They showed clearly that obstruction, when the vertex was on the perineum, was not at the ischial tuberosities, but at the level of the midplane, or above.

Operations of necessity which were performed among the 592 delivered women were: low forceps, 73; midplane forceps, 21; and craniotomies, 3. The majority of low forceps operations were performed on patients anesthetized by caudal or spinal block. The midplane forceps operations tended to occur in cases of pelvic contraction, and all 3 craniotomies occurred in women with combined inlet and midplane contractions.

Cesarean section was performed 19 times on 18 of the 592 delivered women, an incidence of 3.2 per cent. The incidence for the entire service during the same period was 0.55 per cent. The higher incidence in the former group was occasioned by the fact that the pelves of most of the patients submitted to cesarean section were measured radiographically, thus including them in the present series. Elective abdominal delivery, without antecedent labor, was performed either for indications other than cephalopelvic disproportion, or in those with obviously severe contraction. Moreover, since trials of labor were continued into the second stage, either extraperitoneal section or cesarean hysterectomy became the operation of choice following trial labor.

No maternal deaths occurred in the series. There were 26 fetal deaths, 14 of which were related to cephalopelvic disproportion or which were unexplained. There was a tendency for fetal deaths to occur in cases of less than average pelvic capacity.

The author enumerates the criteria of suspicion indicating the necessity for

pelvis may be disturbing on first thought, but all the accepted procedures appear to yield a degree of accuracy which exceeds the requirements of the clinical problem at hand. Thus, Weinberg and Scadron (Am. J. Obst. & Gynec. 52: 255, 1946) measured the pelvis of each of 100 patients by 4 different radiographic methods and the results checked within 0.1 cm.—Ed.)

THE PRESENT STATUS OF CONTINUOUS CAUDAL AND SPINAL ANALGESIA IN OBSTETRICS

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M. Clinics North America 32: 1683-1697, (November) 1948

Anything that concerns the birth of a baby or the welfare of the expectant mother is the target for a great deal of publicity. And when too much publicized, it is frowned on by the medical profession and is condemned before it is given a fair trial. Such was the case with the presentation of continuous caudal analgesia which was heralded by the press even before it was presented to the profession.

Early in the development of continuous caudal it was realized that though it was a beneficial addition to the technics for the relief of pain in childbirth, it was not a method to be used promiscuously or by untrained individuals. The contraindications have been stressed by the author since 1943. They are gross deformities of the spine, tumors that narrow the spinal canal, local infections around the sacral hiatus, skin infections anywhere on the body (to be evaluated by the physician), history of sensitivity to the analgesic agent, profound anemia, placenta previa, floating head, syphilis with probable central nervous system lesions, obese persons, dwarfs and midgets, and pilonidal cysts.

The author reviews the history of the presentation of continuous caudal analgesia and summarizes the results obtained on 2516 labors studied at the Philadelphia Lying-in Hospital. In this group 90.4 per cent received complete relief from pain; 4.3 per cent partial relief; 5.3 failed to obtain relief.

The average duration of the management of primiparous patients with this technic was 3.6 hours of the total 11.6 hours of labor. The multiparous patient was managed 2.3 hours. The incidence of morbidity was 7.4 per cent as compared with 10.8 in the control group. Hypotension was a frequent occurrence in the earlier studies and was overcome by the use of vasopressor drugs, 100 per cent oxygen and elevating the legs to right angles to the body. The incidence of operative deliveries was 68.3 per cent; 56.4 in the control group.

The only infections occurred at the injection site and no such infections have occurred since 1944. No neuropathies were found in the follow-up study.

Of the babies delivered under continuous caudal analgesia, 3.6 per cent had

The clinician must avoid placing too much confidence in pelvic measurements alone. The late Dr. DeLee said, "Since the x-ray cannot measure the strength of the pains, the moldability of the head, or the expansibility of the pelvic joints, or the mutation of the sacrum, or the rigidity of the soft parts, or the metabolism of the parturient, et al., you can see what a small role it plays in the routine of delivery. But I would not be without it."

There has always been a hopeful intent to produce a rule of thumb procedure in which, if accurate measurements were taken, the exact outcome of labor could be calculated. This is, of course, not possible. And a clinician may have a false sense of security when the measurements are normal and forget that even borderline disproportion is a cause for dystocia in only a small number of cases.

The ability to study the pelvic classification and fetal-pelvic relationships far transcends the importance of the pure measurements. Thus the x-ray calls attention to the variations of shape and size which may give trouble and puts the obstetrician on his guard. In cases of borderline disproportion, one must take into consideration such factors as the condition of the mother, the endocrine background and the age, which determine whether or not one should resort to cesarean section or permit a trial labor.

The x-ray should complement the examination, not supplant it. It is because so much has been claimed for pelvimetric methods alone that the procedure has come into disrepute with so many obstetricians.

The author discusses the technic of pelvimetry which he has found best. For mensuration, a pelvimeter which is a modification of a Weitzner rule and consists of an opaque metal ruler with true centimeter scale perforations, is used. The ruler is mounted on a swivel arm and attached to a calibrated stem. Thus it is always parallel with the film. It will have the same distortion as the diameters on the same level.

The film examination includes the following projections; a stereoscopic antero-posterior film of abdomen and pelvis, an erect lateral film, a recumbent soft tissue lateral film, an occasional anteroposterior film of the sacrum and pubis and in breech presentations the recumbent lateral film made with the ruler at the mid-point of the fetal head. All films are taken at a 36-inch skin distance with par-speed double intensifying screens using the Potter-Bucky diaphragm. The range of factors used for the film exposures is given.

In 250 cases seen at Jefferson Hospital over a period of 2 years 25 per cent showed some disproportion, but most of these were borderline. The negative evidence in the remaining 75 per cent was of equal importance. In none of the borderline cases did x-ray alone determine the necessity for operative delivery. 8 figures.

(In connection with the opinions expressed in the above editorial note the last sentence in the abstract of Swenson's article is worthy of reemphasis: "In none of the borderline cases did x-ray alone determine the necessity for operative delivery." This is as it should be.

The author refers to a special technique of x-ray mensuration which he employs. The fact that there are a number of different methods available for roentgen mensuration of the

PREMEDICATION AND ANESTHESIA IN OBSTETRICS: CURRENT PRACTICES AT THE BOSTON LYING-IN HOSPITAL

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New England J. Med., 239: 429-433 (Sept.) 1948

At the Boston Lying-In Hospital there has been an evolution through various developmental phases of anesthesia. The keynote has always been the practice of safe relief of pain, permitting the obstetrician to carry on a conservative policy in the conduct of labor. Certain factors have been especially stressed, the first of which is the close integration of the obstetrical team. Secondly, there has been complete individualization of selection of agents, dosage and route of administration. Thirdly, it is felt that the ideal agent or combination of agents which would meet all requirements is still unavailable. The most successful methods at present all include the use of scopolamine. The judicious use of inhalation anesthetic agents is in general more satisfactory than the analgesia drugs, having the advantages of rapidity of exchange, short induction and recovery period, predictable and controllable depth and duration of anesthesia, retrievableness without residual injury, wide margin of safety, lack of extra load on the detoxifying mechanisms of the body, and permissibility of employment of highly oxygenated atmosphere.

In uncomplicated vaginal deliveries, the following routine is usually employed. One tenth gm. of seconal is given early in labor to determine sensitivity, and if no untoward reactions are encountered, 0.1 gm. of seconal and 0.1 gm. of amytal are given by mouth or rectum. At the same time, 0.6 mgm. of scopolamine hydrobromide is administered intramuscularly. As labor progresses, 0.4 mgm. of scopolamine and 1.2 mgm. of apomorphine are given at 2-hour intervals. The delivery is completed under an inhalation procedure employing a highly oxygenated atmosphere until delivery of the fetus is completed. Careful observation is maintained while the patient recovers consciousness.

Certain special problems arise which require additional consideration. In the presence of respiratory complications such as upper-respiratory-tract infections the barbiturate dose is reduced by one half. Delivery is completed under the plan of premedication or supplemented with regional block. In patients with asthma, the barbiturates are reduced so as not to exceed 0.2 gm. of seconal, and scopolamine and apomorphine are given as described. The delivery is completed under inhalation anesthesia, the agent and the drugs having first been studied by a skin test. Patients with active tuberculosis are treated the same as patients having acute respiratory tract infections.

Both premedication and anesthesia are individualized for patients with Class IA cardiac disease (unfavorable cardiac case). For those in Class I (favorable cardiac cases), demerol in doses of 50 to 100 mgm. is administered intramuscularly and delivery is completed under inhalation anesthesia. In Classes II and III

respirations delayed beyond 2 minutes as compared with 9.6 per cent in the control group.

The results in 161 cases of the use of the caudal technic in cesarean section were very satisfactory. It was useful in cases where the cesarean section seemed indicated earlier and the analgesia could be continued for the operation and in cases of severe pre-eclampsia.

The author cautions that although continuous caudal cannot be termed a *terminal analgesia*, it is best used only 3 or 4 hours before expected delivery and always in the presence of strong uterine contractions. He feels that this technic has not yet received a fair trial by many of its critics.

A brief history of the use of spinal anesthesia in surgery and obstetrics is given. The fractional spinal anesthesia, the availability of drugs of less toxicity, such as procaine, metycaine and pontocaine, and the use of smaller doses have played a part in the present day successful use of regional anesthesia. The author reports that cesarean sections and vaginal deliveries have been done painlessly on doses as small as 15 mg. of metycaine. He suggests the giving of the drug between the first and second interspaces instead of the third and fourth.

Nine out of 10 of the cesarean sections done at the Chicago Lying-in Hospital are now being performed with spinal anesthesia and the increase in its use is also demonstrated by the fact that only one was given at the Mayo Clinic in 1921 while 11,000 were given in 1944.

If the proper technic is strictly adhered to, the hazards to which the patient is exposed are minimized. In the last 100 cesarean sections done with fractional spinal anesthesia, an intravenous drip of 0.5 per cent pentothal sodium in glucose, running at the rate of 45 drops a minute, was administered until the baby was out of the uterus and increased to 90 drops thereafter, allowing the already relaxed patient to sleep during the rest of the operation. Until the actual delivery of the child the mother is conscious. The amount of pentothal used has no effect on the child and this technic has been successful.

There is an increasing number of vaginal deliveries being done with spinal anesthesia with good results. Just as with the continuous caudal there are the usual precautions to be observed. For those not well experienced in the block technic it is wise to limit the use of it to the semi-terminal stage only.

The control of the level of anesthesia, the proper dosage of the drug, frequent blood pressure readings, the use of low forceps and the correction of postspinal headaches are discussed.

(This article, based upon a large experience with conduction anesthesia in obstetrics, contains many practical points. To single out just one, the use of an intravenous drip of 0.5 per cent pentothal sodium in glucose in conjunction with continuous spinal anesthesia adds much to the composure of the mother but, in this low concentration, does not appear to affect the baby.—Ed.)

cations. A careful spinal tap is done and if the tap is bloody or if an allergic reaction to procaine is noted, the procedure is discontinued. For pelvic delivery, procaine hydrochloride, 50 to 100 mgm. in concentrations not over 5 per cent, is used with spinal fluid as the diluent. For abdominal deliveries, 100 to 150 mgm. of procaine hydrochloride is used and the duration of analgesia is usually one to 1½ hours. During the procedure the blood pressure, pulse and respirations are checked at 5-minute intervals and the patients are watched for signs of intercostal breathing, pallor, disorientation, nausea and emesis, thirst, air hunger, palpitations, precordial distress and psychosomatic complaints. Supplementary anesthetic agents and supportive measures are employed when necessary. Only 20 per cent of the cases at the Boston Lying-In Hospital receive other than inhalation anesthesia. Ether is the agent of choice in an oxygen-enriched atmosphere.

(The author of this paper is an obstetric anesthesiologist of great experience, especially in the inhalation field. The country over, barbiturate and scopolamine analgesia followed by inhalation anesthesia, is unquestionably the most widely used method of pain relief in obstetrics, and by and large has given most satisfactory results. Of the several methods available nowadays, that program is the most certain in its effects, the incidence of complete failures being decidedly less than with conduction anesthesia even when the latter is in fairly competent hands. There is a certain proportion of patients, moreover, who prefer to go to sleep during labor and still another fraction in which conduction anesthesia is contraindicated. In other words, despite the inroads which have been made by conduction anesthesia, systemic methods of pain relief in labor still have an important place in our armamentarium; and their uses and contraindications are sanely and lucidly set forth in the above article on the basis of the extensive experience which the author has had with them at the Boston Lying-in Hospital.—Ed.)

OBSERVATIONS ON THE ROOMING-IN PROGRAM OF BABY WITH MOTHER IN WARD AND PRIVATE SERVICE

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Am. J. Obst. & Gynec. 57: 176-186 (Jan.) 1949

On July 12, 1947, the policy of rooming the normal, full-term, newborn baby with its mother was inaugurated in the obstetric wards of the Jefferson Medical College Hospital. From that time until April 12, 1948, which represents the period covered by this study, 1018 newborn babies were cared for in this fashion. Of these, 926 were the offspring of ward patients; 92 were the babies of private patients who were cared for in a low-cost, semiprivate ward. The ward service consists of 6 rooms, each containing 6 beds.

Babies are kept in cribs at the mother's bedside both day and night unless one or the other is ill, or unless at night an individual baby is unusually noisy.

At first, the equipment for the care of the mother's breasts and of the baby was

cardiac disease (functional), the patients are treated like the uncomplicated vaginal delivery cases, with careful observation for untoward manifestations.

If moderate to mild impairment of renal function exists, the dosage of the drugs used for premedication is reduced to one half and delivery is completed under inhalation anesthesia. If more severe damage exists, the premedication is further reduced or omitted and delivery is completed under regional analgesia.

If the patient has eaten immediately before labor starts the "full stomach" is emptied by washing or by a larger initial dose of apomorphine. If the stomach has not been adequately emptied at the time of delivery, a regional analgesic block is employed. Patients are not permitted food and fluids during labor, necessary fluids being administered parenterally. In cases requiring operative abdominal surgery, the premedication and anesthesia are individualized.

In the central nervous system complications, the premedication and anesthesia are usually the same as in the uncomplicated case, but individualization is again necessary. Regional analgesia and the use of solid anesthetic agents are contraindicated in this group of cases.

In diabetic patients, the plan of premedication is essentially the same but the dose is reduced so as to avoid unconsciousness. Labor is terminated with regional block.

In hyperthyroidism the dose of premedication is increased and labor is completed with inhalation anesthesia.

For patients who are to have a cesarean section or a "double set-up," 0.2 gm. of amytal and seconal are given 2 hours before and 0.6 mgm. of scopolamine and apomorphine one hour before operation. Inhalation anesthesia is usually used. If prematurity or immaturity is suspected, the amount of premedication is reduced and regional block is employed. If a test of labor is attempted, the dosage of premedication is cut in half and inhalation anesthesia is the method of choice. In patients with mild pre-eclampsia or eclampsia, the routine for uncomplicated deliveries is followed. The more severe cases are individualized, but demerol is usually the premedication of choice. In these cases an attempt is made to deliver the patient under the premedication alone or with the use of light inhalation anesthesia. Intravenous anesthesia and nitrous oxide are contraindicated.

Spinal analgesia is employed if one or more of the following complications exist: respiratory complications, a full stomach, fetal distress when further depression is best avoided, prematurity or immaturity of the fetus, diabetes mellitus, and other complications such as surgical procedure other than obstetric. Contraindications to spinal analgesia include tumors, hemorrhage into or syphilis of the central nervous system, pernicious anemia and other lesions of the central nervous system, infections of the skin at the site of injection, history of headache or backache, psychoses and psychoneuroses, congenital abnormalities around the spinal column, anemia, cardiovascular disease, labile vasomotor system, malnutrition, septicemia, hemorrhage or shock, allergy to solid anesthetic agents, obesity, serious uterine complications and abnormal spinal fluid findings. If regional anesthesia is contemplated, amytal and demerol are given as premedi-

taining a fresh change of clothing for the baby, fresh materials for the crib, baby blanket, and a sterile sheet of paper for weighing on the scales. Ward rounds are then made by the nurses from the central nursery employing a ward carriage equipped with scales, antiseptics, dressings for the navel, thermometers, and emergency drugs. As this equipage comes along, the mother undresses her baby on her bed, changes the linen in the crib, puts the sterile sheet of paper on the scales, and watches her baby being weighed. She also watches the cord dressing changed and is instructed in the cleansing of neck, axilla, groin, vulva, with sterile swab and sterile water. Most mothers, even multiparas, are surprised and rather concerned at the presence of the stump of umbilical cord, never having noted it before in the course of baby care. Upon the occasion of these morning rounds, the nurses make their records of the baby's weight and temperature, and obtain from the mother's record of the previous 24 hours the data concerning nursing periods and baby's bowel movements. Twice in the course of her 8 hour duty, the graduate in charge of the nursery makes rounds and personally checks on all babies. In the meantime, the babies are under almost constant observation of the floor nurses.

This system has satisfied the requirements for which it was set up, i.e., there have been no ill babies among these house-in babies, and there have been no epidemics among the newborn. The care of the baby has also been simplified and there has been no addition of nursing hours. The babies have seemed to be contented and happy under this arrangement, have gained rapidly in weight and the percentage of breast feeding has increased. The mothers have in general enjoyed having their babies with them. They have learned to take care of the baby from the first postpartum day on and have left the hospital quite capable of managing the ordinary problems of infant care. The arrangement of housing baby with mother has been found to depend for its success to some degree upon early ambulation and breast feeding, and, in turn, the housing-in arrangement aids in involution and encourages breast feeding. The plan also seems to work particularly well in small wards where mothers can watch each other, teach each other, and can be under the frequent observation of the nursing personnel. The question of how well this plan will work in the private and small semiprivate rooms has not been adequately answered. However, the authors see no reasons why the plan will not work there, too, if the proper modifications and adjustments are made.

placed on a central table in each ward but it was soon observed that this arrangement would permit of cross-infection, and was also inconvenient to mother and nurse. In order to overcome this difficulty, a small crib-wardrobe was designed which the hospital carpenter constructed and which is hung on the end of each baby's crib. The crib-wardrobe consists simply of an upper and lower shelf. The top shelf contains covered jars for alcohol sponges, water sponges, dry cotton balls, and used sponges. The larger lower shelf contains the supply of individual diapers, pads, and blankets for a day's usage.

With this arrangement, the mother can readily reach her baby and the materials for its care while she is lying in bed or sitting on the edge of the bed; and no one touches these materials except herself. The wardrobe can be readily lifted from the end of the crib and is constructed without covers or drawers so that it is easily and thoroughly washed with soap and water. This arrangement has worked most successfully, at an expenditure of not more than 5 or 6 dollars per crib, and has made it possible for us to provide quite efficiently for the individual care of each baby.

Healthy, normal, full-term babies are placed with their mothers very soon after delivery. If the baby has considerable mucus in its pharynx, it is kept in the central nursery until this has cleared and respiration is normal. If the delivery is during the night, the baby may not be placed with the mother until the next morning. In not a few instances, however, the baby is at the mother's bedside within 2 to 3 hours after delivery. The practice is for the attendant in the delivery room to call the ward nursery when a delivery is completed and the newborn baby's condition determined to be satisfactory by the attending obstetrician. An individual stand, crib, and wardrobe are then prepared and the baby transported by the nursery attendants to its freshly prepared habitation in the nursery. Within a short time, with the exceptions mentioned above, the baby is beside the mother in the ward. Baby and mother are generally ready for this intimate association at an early hour for the authors employ little sedation during labor, light inhalation anesthesia for delivery, and local anesthesia for episiotomy and repair.

During the first 24 hours after delivery, the nurses take a great deal of time with these patients, demonstrating the technic of nursing and of baby care, and emphasizing constantly the importance of cleanliness. The mother is encouraged to move freely in bed and participate in these various activities, but ordinarily she does comparatively little for her baby during the first 24 hours other than observe its progress.

By the end of 24 hours, the mother is generally out of bed, and thereafter conducts practically all of the routine care of herself and of her baby. She goes to the lavatory, uses the central wash basin, and sits either on the bedside or on a chair by her baby's crib. She calls upon the nurse in case of question or difficulty, but she learns very quickly to manage all ordinary situations and ordinarily gives her offspring excellent attention. From that time on until discharge, the nurses have very little to do with respect to feeding or changing of the baby.

Each morning the mothers are supplied with an individual "bath pack" con-

(Zentralbl. f. Gynäk. 57: 1180, 1933). He encountered an error of only 5 per cent and other authors have confirmed the dependability of the test as of that general order in research series.

Nitrazine Test. The use of the indicator substance, nitrazine, for the diagnosis of ruptured membranes was first suggested by Baptisti in 1938 and is a simple and fairly reliable method (Am. J. Obst. & Gynec. 35: 688, 1938). Baptisti used indicator test papers impregnated with the dye. With these papers is furnished a color chart comprising a pH range from 4.5 to 7.5 (made by E. R. Squibb and Company). The papers are set at pH of 6.0. These indicator papers were intended for use primarily to determine the reaction of urine. The pH of the vaginal secretion was determined by inserting a sterile cotton tipped applicator deeply into the vagina, and after withdrawal, the cotton tip was touched to a strip of the nitrazine paper and the paper then compared with the color chart. Color changes of olive green to yellow indicate a pH on the acid side and point to intact membranes whereas varying shades of blue indicate a pH of more than 6.0 and are evidence of ruptured membranes. Baptisti points out that a false reading is likely to be encountered in patients with intact membranes but who have an unusually large amount of bloody show since the blood, like amniotic fluid, will tend to turn the indicator to the alkaline side. His results in 50 consecutive cases were generally satisfactory.

A more extended study of the nitrazine test by a slightly different technique was made by Abe in 1940 (Am. J. Obst. & Gynec. 39: 400, 1940). Abe's technique was as follows. Ordinary cotton applicators are dipped in nitrazine test solution and then dried. Upon evaporation the dye yields a canary yellow color with scattered streaks of green. This is the neutral point at about pH 6.6. A dyed cotton applicator and a short glass tubing, the purpose of which will be explained later, are placed in a large sized test tube and stoppered with a cotton plug. This is then autoclaved. The test tube container is used purely for convenience, as it can be kept in the labor room for immediate availability or carried around as part of the doctor's equipment. After proper antisepsis of the vulva, the labia are widely separated and the sterile glass tubing (0.5 in diameter and 3.5 inches long) is inserted into about one-third distance of vaginal tract. Through this tubing the dyed applicator is passed until it approaches the site near the external os where amniotic fluid should be of the greatest concentration if rupture of the membranes has occurred. Thus, the glass tubing has a 2-fold purpose: to allow a sterile introduction of the dyed applicator high into the vaginal vault, and to obtain a correct pH reading of the vagina not affected by urine which may have trickled down over the introitus. The applicator is left in the vagina for 30 seconds, removed, and the change in color is noted. Interpretations of the color changes are as follows:

Yellow.....	pH 5.0}	Intact membranes
Olive yellow.....	pH 5.5}	
Olive green.....	pH 6.0}	
Blue green.....	pH 6.5}	Ruptured membranes
Blue gray.....	pH 7.0}	
Deep blue.....	pH 7.5}	

Abe reported 176 cases in which the nitrazine test was used according to the technique described and found it correct in 98.9 per cent of patients with known rupture of membranes and in 96.2 per cent in patients with intact membranes. Abe, as well as Kushner (Am. J. Obst. & Gynec. 38: 1046, 1939), found that nitrazine was a more accurate indicator for the purpose at hand than was bromthymol blue. We have employed nitrazine papers for the diagnosis of ruptured membranes ever since they were first suggested by Baptisti and have found the test easy to carry out and reasonably dependable. It must not be thought, however, that the ordinary clinical use of these pH tests will yield as good results as those reported above because the practical employment which is usually made of the procedure

THE DIAGNOSIS OF RUPTURED FETAL MEMBRANES BY USE OF A SIMPLIFIED VAGINAL SMEAR TECHNIQUE

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J. Am. M. Women's Ass., 3: 498, (Dec.) 1948

It is often important to have some way of determining, with some degree of certainty, if the fetal membranes have ruptured, and frequently the mother cannot be certain. The choice of the type of obstetrical operation may depend on the status of the fetal membranes in order that contamination may be prevented. In other instances where rupture is suspected the decision of whether to induce labor or to let nature take its course would be influenced by the knowledge that amniotic fluid was escaping or that the membranes had sealed over.

The authors have described a simplified vaginal smear technique which is helpful in ascertaining if the membranes are intact or not. The specimen is taken with a dry, sterile bulb pipette and fixed in ether and alcohol. It is then stained at the convenience of the operator, using the Shorr single differential stain. The taking of the specimen and staining of the preparation takes only 6 to 8 minutes and requires no special training.

The diagnosis is made by identifying fetal squamas (stratified squamous epithelial cells in varying stages of disintegration) in the vaginal smear. These squamas are sufficiently characteristic so as to be recognizable by an amateur cytologist after a short period of study. The fetal squamas are faintly staining squamous cells having a tendency to form groups or sheets and to cytoplasmic and nuclear degeneration. They stand out in contrast to the vaginal epithelial cells with which they are admixed. The presence of abundant fetal cells is considered positive evidence of rupture of the membranes.

The results of 75 random cases were presented in this study. There was a 79 per cent correlation between history and smear. Among the positive histories, there was an 89 per cent correlation, and of the negative histories, there was a 77 per cent correlation. Two cases in which the history was unreliable showed a positive smear and 2 other such cases had a negative smear.

(The clinical diagnosis of ruptured membranes may sometimes be surprisingly uncertain and a number of tests to decide the question have been recommended.

One of the first procedures to be suggested was that of Philipp which was based on the microscopic demonstration of lanugo hairs in fluid obtained from the vagina (*Zentralbl. f. Gynäk.* 53: 16-18, 1929). Because of difficulty in finding lanugo hairs and in differentiating them from other fibrils that may occasionally be encountered in the vagina, this test has not enjoyed appreciable usage.

Perhaps the most widely employed procedure is one or another method of testing the acidity or alkalinity of the vaginal fluid. These tests are based on the fundamental fact that the normal pH of the vaginal secretion ranges between 4.5 and 5.5, whereas the pH of the amniotic fluid is usually 7.0 to 7.5. In 1933 Temesvary applied this circumstance to diagnostic use and reported 131 cases in which bromthymol blue was used as an indicator

PATHOLOGY OF PREGNANCY

A COMPARISON OF INTRAVENOUS OXYTOCIN AND ERGONOVINE IN THE CONTROL OF HEMORRHAGE ATTENDING DELIVERY

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South. M. J., 41: 980-987, (Nov.) 1948

Postpartum hemorrhage as a cause of maternal death has shown little decline in the past 10 years as compared with other leading causes, namely infection and toxemia. With the recognition of the effects of ergot and pituitary extract on the uterine muscle, 2 potent agents in the control of hemorrhage in labor were made available. It is the purpose of this paper to compare the 2 drugs, ergonovine and oxytocin, used intravenously, in respect to the following observations: (1) rapidity of oxytocic effect; (2) amount of blood lost; (3) frequency of contraction ring with retained placenta; (4) manual removal of placenta; and (5) any unfavorable general reactions shown by the patient.

For purposes of this investigation, 2 sets of sheets were placed in the delivery rooms; on the back of each sheet was written the word "pitocin" or "ergotrate" to make a total of 100 sheets for each drug. In the delivery room, the nurse prepared whichever drug was to be used at the end of the second or during the third stage, without the attendant's knowledge of what was to be given. Prior to draping, 2.5 units of "pitocin" was given subcutaneously, if "pitocin" was to be used intravenously during the third stage; or pituitary extract, 2.5 units, subcutaneously, if ergonovine was to be given at the end of the second stage. Paraldehyde amnesia was routinely used, and episiotomy was almost a routine procedure.

At the moment of delivery of the anterior shoulder, the nurse injected intravenously 1 cc. of undiluted ergonovine maleate, or immediately following birth of the baby she injected intravenously 2.5 units of undiluted "pitocin," the remaining 7.5 units being injected subcutaneously. Following delivery, the operator grasped the uterine fundus and noted the exact time required from injection to contraction of the uterus in response to the injection. Following this, the baby was cared for, and the placenta was then expressed. Pituitary extract or oxytocin, 7.5 units, was given subcutaneously. Before the patient was returned to her room, 0.2 mg. of ergonovine was given intramuscularly to both series of patients.

The average time required for oxytocin to produce a uterine contraction was 30.9 seconds. The average time for ergonovine to produce oxytocic effect was 54.3 seconds. Very little difference was noted in the length of the third stage whether oxytocin or ergonovine was used, the average time being 7.17 and 6.73

*Through printer's error on the page proof, this abstract was placed in this section instead of in the section dealing with the management of normal pregnancy, labor and puerperium.

is to test borderline cases in which the amount of fluid present is small and, since it is small, may sometimes be affected by the pH of the vaginal secretions. As has been pointed out, moreover, admixture of blood with vaginal secretions may lead to an erroneous diagnosis of ruptured membranes.

Fat Globules. The demonstration of fat globules microscopically in the vaginal fluid is another fairly dependable test but is somewhat more troublesome to carry out than the nitrazine techniques. It was first recommended by Numers in 1936 (*Acta obst. et gynec. Scandinav.* 16: 249, 1936) and is used in a number of clinics. The technique is as follows. A speculum is inserted one or 2 cm. above the introitus; one drop of secretion is taken and spread out on a clean slide. The preparation is air-dried and, without previous fixation, stained at room-temperature in a dye-solution, obtained by dissolving 0.2-0.3 grams Sudan III in 100 cc. 70 per cent hot alcohol. The slide is washed in water, dried by blotting-paper and examined immediately after the staining under low magnifying power. The fat-substances are stained a distinct orange-red; particles of mucus are sometimes stained weakly yellowish-red. These, as well as small, faintly tinted drops of fat occurring in expelled cells of the vaginal epithelium, may be easily distinguished from the fetal fat-substances. In all, 280 cases were examined by Numers, 141 of them before the rupture of membranes and 139 afterwards. Only 4 of the former cases gave a slight positive Sudan reaction, the rest yielding a negative result (97.2 per cent). The samples taken after the rupture of membranes gave a positive outcome in 99.3 per cent; one negative case only was observed. Slight Sudan reactions seem to be relatively more frequent in premature cases. The faulty reactions amount to a round 2 per cent of the entire material.

Fetal Epithelium. Still another test is based on the demonstration of disintegrating squamous cells from fetal epithelium as proposed first by Bourgeois (*Am. J. Obst. & Gynec.* 44: 80, 1942) and as described in the above article by Taylor and Roberts. Either the Shorr differential stain or some modification of it is used. The morphologic differentiation of fetal squamas from sheets of cells recently desquamated from the maternal vagina, vestibule, or urethra, is made on the fact that cells from those locations generally possess well developed nuclei and granular cytoplasm which lacks the translucence of vaginal cells. Bourgeois reported an overall accuracy of 97.1 per cent in 344 specimens of vaginal fluid from 275 patients. It should be noted, nevertheless, that characteristic fetal squamas are not consistently found in liquor amnii prior to the beginning of the ninth lunar month.

The fact that these several techniques for the diagnosis of ruptured membranes have been recommended is indication enough that no one of them is without its drawbacks. Thus, the pH methods may be vitiated by admixture of blood and are less dependable when only minute quantities of amniotic fluid have escaped. The identification of fetal epithelium becomes of little value prior to the thirty-second week. This test, moreover, demands some little training in cytology since degenerating squamous epithelium, both from fetal and vaginal sources, may be encountered and they tend to converge in their morphology. The demonstration of fat globules, like that of fetal squamas, is more uncertain prior to the thirty-second week since the amount of vernix is much less. In other words, both these microscopic tests are of little value before the ninth lunar month.

In summary, the nitrazine test is certainly the simplest of the various procedures and, if allowances are made for the sources of error mentioned, is as accurate as any of the others. If, in a given case, there is reason to question it, the fat globule test is probably the next most practical.—Ed.)

nerve block. The authors indicated that hypertensive crises and convulsions were controlled instantaneously with the proper applications of continuous caudal analgesia and continuous spinal anesthesia with the catheter technics. They concluded that the relief of angiospasm in the lower half of the body removes a considerable load from the heart, thereby reducing the danger of cardiac insufficiency and pulmonary edema and the possibility of intracranial hemorrhage. The associated vasoconstricting effect of eclampsia on the kidneys is relieved, thereby increasing the renal blood flow and urinary output. The suprarenal gland is denervated with the extension of the block to the sixth thoracic segment.

The case in question, which is one from a large series, was a 17-year old primigravida who was admitted to the hospital because of convulsive seizures. Five convulsions were noted within the four hours preceding admission. Her blood pressure was recorded at 180 systolic and 110 diastolic. The pulse and respirations were rapid, the tongue was lacerated, and the patient was semicomatose. There was a 3-plus proteinuria.

The patient was sedated according to the modified combined therapy of Dieckmann, consisting of .3 gram of sodium luminal and 2 cc. of 50 per cent magnesium sulfate by intramuscular injection, and 20 per cent hypertonic glucose in 500 cc. of distilled water intravenously. Within an hour the patient had her sixth convulsion. Accordingly, 8 ccs. of 1.5 per cent metycaine was injected as a test dose. After 5 minutes with no evidence of spinal anesthesia, an initial dose of 22 cc. was administered. The blood pressure gradually fell to lower levels, averaging 140 systolic and 90 diastolic. The segmental level of cutaneous analgesia was maintained between thoracic 8 and 10. Twenty cc. of metycaine solution every 45 minutes was established as the maintenance dose. Regional nerve block was thus maintained and the blood pressure controlled for the next 36 hours, after which time the caudal block became gradually ineffective even upon substitution of .15 per cent pontocaine.

Active labor was initiated by artificial rupture of the membranes. Since the blood pressure was mounting, satisfactory nerve block was reestablished by the institution of continuous spinal anesthesia with the catheter introduced into the subarachnoid space through the Tuohy spinal needle cephalad for 10 cm. from the skin surface in the third lumbar interspace. Doses of 1.5 per cent metycaine of from 1 to 2 cc. each hour resulted in satisfactory control of the blood pressure, and afforded complete pain relief.

The uterine contractions were unabated and cervical dilatation progressed rapidly during the first hour of this nerve block. Satisfactory delivery of a normal female infant was completed with low forceps and episiotomy. Thereafter, the nerve block was continued for 24 hours. By this time, since the blood pressure was within a safe range, the injections were stopped but the indwelling spinal catheter was left as a prophylactic measure. This systolic blood pressure did not ascend to levels above 150 mm. of mercury. During the sixth to eighth postpartum day there was fever as high as 102 degrees Fahrenheit. The infection was determined to be in the urinary tract, and fever promptly subsided with penicillin therapy, permitting discharge of both mother and baby in good condition on the 11th postpartum day.

minutes, respectively. The routine of caring for the baby before expressing the placenta no doubt accounted for the increase in the length of the third stage in this series.

The average blood loss for each drug was essentially the same, being 192.9 cc. with oxytocin and 197.7 cc. with ergonovine. Of the patients who received oxytocin there were 9 (9 per cent) who developed contraction ring and in 4 of these cases it was necessary to remove the placenta manually. Two of these patients with contraction ring lost 700 cc. of blood, one of whom required manual removal; 2 patients lost 450 cc., one of whom required manual removal; 4 patients lost between 300 and 400 cc.; 2 of whom required manual removal; and one patient lost only 100 cc. of blood. Two patients (2 per cent) in the ergonovine group developed contraction ring. One of these required manual removal of the placenta but lost only 100 cc. of blood. The other patient lost 275 cc. of blood.

There is no apparent justification for the belief that undiluted oxytocin given intravenously causes severe generalized reactions. No such reaction has been seen in more than 4000 personally observed cases. Ergonovine given intravenously occasionally produced noticeable cyanosis of the chest, neck, head and arms, but apparently without serious general effect.

Of the patients receiving oxytocin, 39 per cent sustained a blood loss of less than 100 cc., as compared to 37 per cent of those receiving ergonovine. However, 10 per cent of the oxytocin series lost between 300 and 400 cc. of blood, as compared to 6 per cent of the ergonovine series. The greater frequency of contraction ring and manual removal of the placenta with the use of oxytocin no doubt accounted for the greater quantities of blood lost.

The writers conclude that both oxytocin and ergonovine should be prepared in sterile syringes and be available for intravenous injection at the moment or directly after the birth of the baby, if deemed necessary. Although there is a definite increase in frequency of contraction ring following the intravenous use of either of these drugs, particularly oxytocin, in well equipped maternity hospitals the lessening of blood loss may be considered to outweigh the disadvantage of increased frequency of contraction ring. Since intravenous oxytocin produces oxytocic effect in half the number of seconds required for ergonovine, it is therefore preferable in actual or potential postpartum hemorrhage.

THE TREATMENT OF ECLAMPSIA BY MEANS OF REGIONAL NERVE BLOCK

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South. M. J. 41:920-922, October, 1948

From Memphis, Tennessee, comes a sample case report of eclampsia managed successfully for more than 60 hours with two types of conduction anesthetic

TABLE 1

CASE NO.	AGE	COLOR	PARITY	WEIGHT	NO. CONVULSIONS	MAX. & MIN. B.P.	TYPE OF BLOCK	METHOD OF DELIVERY	CONDITION OF BABY	OUTCOME OF PATIENT
1	15	B	1	117	2	200/140 150/130	Caudal	C.S.	Lived	Lived
2	23	B	0	158	1	140/90 95/50	Caudal	L.F.	Lived	Lived
3	18	B	1	121	1	195/120 100/70	Spinal	Spon.	Stillb.	Lived
4	23	B	5	101½	1	200/150 130/90	Caudal	Spon.	Lived	Lived
5	18	B	1	—	2	210/140 140/110	Caudal	C.S.	Lived	Lived
6	17	B	1	126½	1	200/130 130/90	Caudal	Spon.	Lived	Lived
7	26	W	1	—	2	190/120 110/70	Spinal	C.S.	Lived	Lived
8	17	B	1	107½	1	190/90 120/70	Caudal	Breech	Lived	Lived
9	18	B	1	166	2	190/130 90/60	Spinal	L.F.	Stillb.	Lived
10	15	B	1	143½	2	220/130 128/116	Caudal	L.F.	Lived	Lived
11	17	B	1	131	1	190/130 116/90	Caudal	L.F.	Lived	Lived
12	24	B	3	110	2	205/125 120/80	Caudal	C.S.	Lived	Lived
13	21	B	3	126½	1	190/156 120/80	No block	Spon.	Lived	Lived
14	15	B	1	—	1	180/100 130/90	No block	L.F.	Lived	Lived
15	22	B	2	157	1	190/110 145/90	Caudal	Spon.	Lived	Lived
16	17	B	1	103	2	175/130 110/75	Caudal	L.F.	Lived	Lived
17	23	W	1	160	2	160/130 140/90	Cath. caud.	O.F.	Stillb.	Lived
18	26	W	1	135	1	172/110 126/94	Cath. caud.	M.F.	Lived	Lived
19	22	B	2	123½	5	180/120 140/90	Caudal	Version	Stillb.	Died
20	14	B	1	135	7	175/115 118/74	Caudal	L.F.	Lived	Lived
21	18	B	2	137	4	200/120 140/100	Caudal	Spon.	Lived— twins	Lived
22	16	B	1	—	10	158/90 110/80	Caudal	L.F.	Lived	Lived
23	14	B	1	—	3	170/110 90/60	Caudal-spinal	M.F.	Lived	Lived
24	19	B	1	135	8	210/150 90/65	Spinal	M.F.	Lived	Lived
25	18	B	1	—	5	210/160 160/130	Caudal	C.S.	Lived	Lived

The authors emphasize that regional nerve block was reserved in most cases as a procedure to effectively control blood pressure and convulsions in those cases not controlled with sedation and magnesium sulfate. From their experience they noted that another important application of this method is in the management of severe pre-eclamptic patients in order to prevent the development of the convulsive state.

(During 35 months, from November 1, 1945, to September 30, 1948, in the hospitals of Memphis, Tennessee, there occurred 70 cases of eclampsia under my personal supervision. Sixty-two of these occurred in the John Gaston Hospital in the obstetrical department managed in collaboration with Dr. Frank E. Whitacre and Dr. Henry B. Turner, 5 in the Baptist Hospital, 1 in the Methodist Hospital, and 2 in the St. Joseph Hospital. To this number are herewith reported 4 additional cases of eclampsia which I have managed with conduction anesthesia at the United States Marine Hospital, Staten Island, New York, the Jefferson Hospital in Philadelphia, the Druid City Hospital in Tuscaloosa, Alabama, and at the Brooke General Hospital in San Antonio, Texas. Meticulous analytical data have been tabulated on 48 of these cases. This is presented in the master chart. The minute information on 26 other cases is being tabulated at present for an additional report.

These case histories are presented to substantiate the method of management described in the summary above. These 74 patients were delivered of 76 babies, of which 62 were discharged alive—an infant salvage rate of 81.6 per cent, or an uncorrected fetal loss of 18.4 per cent. In this group there were 9 stillbirths and 3 neonatal deaths. Three of the 74 mothers died, an uncorrected maternal mortality of 3.89 per cent. One of the deaths occurred 19 days after delivery. The patient was in coma from her sixth convulsion throughout this period of time. Her blood pressure was controlled with conduction anesthesia for 8 days. Her urinary output was adequate in volume but of low specific gravity. A second death occurred instantaneously with the injection of 30 mgm. of metycaine through the Tuohy catheter with the patient in the sitting position because of orthopnea. Autopsy revealed an interventricular hemorrhage. The immediate cause of death, however, was too large a dose of the anesthetic agent. The third death resulted 20 hours postpartum from interventricular hemorrhage 18 hours after the nerve block had been discontinued. Table 1 shows the essential information of 48 consecutive cases of eclampsia, which is summarized in Table 2.

Since the manifestations of eclampsia represent a critical, central, and peripheral neurovascular stampede of pathological processes, a prompt and thorough evaluation of the vital organ centers must be made before an intelligent application of therapy. The catastrophic dangers of anoxia to the mother and secondarily to the dependent baby through convulsive strangulation by masseter and pharyngeal tetany must be prevented by the maintenance of an unobstructed airway; pulmonary edema associated with acute cardiac failure must be prevented or correctly treated; cerebral apoplexy as an end result of extreme hypertension must be prevented. Thus, priority should be accorded to the restoration of normal function in the maternal heart, lungs, and brain.

The essentials of management of the processes are:

1. 100 per cent oxygen, sometimes under positive pressure, in pulmonary edema, cyanosis from obstruction, or from inadequate functioning of the neuro-respiratory apparatus.
2. Prompt reduction in venous return to the failing and decompensated heart which is oftentimes laboring under the strain of extreme systolic and diastolic pressures. In the past this was accomplished by phlebotomy and/or pharmacologic vaso-relaxation with veratrum compounds. Now it can be more accurately controlled by conduction nerve block without subjecting the baby in utero to this powerful depression. Likewise, conduction anesthesia, in producing bloodless phlebotomy, through vaso-dilatation for as long as necessary, does not waste blood.
3. Control of the extremes of nervous excitation with moderate sedation and magnesium sulfate already considered in the modified combined therapy of Dieckmann.

In an essential, but at the moment, secondary role is the maintenance of protected liver function and renal function. The management of the liver in toxemia requires:

1. Adequate oxygenation.

TABLE 2

Age:		Caudal & spinal.....	3
Under 20.....	26	Caudal insertion failures.....	6
20-25.....	10	Method of delivery:	
26-30.....	6	Spontaneous.....	18
31-36.....	6	Operative.....	19
Color:		Section.....	11
Black.....	33	Condition of baby:	
White.....	15	Stillbirths.....	9
Parity:		Neonatal deaths.....	3
1.....	30	Discharged alive.....	38
2-5.....	15	Outcome of patient:	
Over 5.....	3	Recovered.....	45
Previous eclampsia:		Expired.....	3
Yes.....	1	Month of year:	
No.....	47	April.....	13
Weight:		January.....	5
More than 140 lbs.....	14	July.....	5
Convulsions:		March.....	4
Only 1.....	10	February.....	3
2-5.....	27	August.....	3
More than 5.....	11	May.....	3
Prenatal care:		December.....	3
No.....	21	June.....	2
Yes.....	27	November.....	2
Hemoglobin:		October.....	1
Over 10 grams.....	21	September.....	0
10 grams & under.....	17	Unknown.....	4
Unknown.....	10		
Edema:			
Yes.....	27		
No.....	21		
Oliguria & anuria:			
Yes.....	20		
No.....	28		
Maximum blood pressure:			
Above 180 systolic.....	32		
140 to 180 systolic.....	16		
Below 140 systolic.....	0		
Type of conduction block:			
Caudal.....	28		
Spinal.....	11		

Of the 26 cases subsequently managed in the John Gaston Hospital, there were no maternal deaths. Twenty-four babies were discharged alive and two were stillborn.

Grand totals

Consecutive cases of eclampsia.....	74
Died.....	3
Lived.....	71
Babies.....	76
Stillborn and died.....	14
Lived.....	62

2. Sufficient glycogen replacement following the abnormal mobilizations from the adrenogenic stimulus of eclampsia.

The management of the kidney in eclampsia so often associated with suppression of urine or complete anuria requires:

1. Adequate oxygenation.
2. Relaxation of the angiospastic mechanism.

TABLE 1—Continued

CASE NO.	AGE	COLOR	PARITY	WEIGHT	NO. CONVULSIONS	MAX. & MIN. B.P.	TYPE OF BLOCK	METHOD OF DELIVERY	CONDITION OF BABY	OUTCOME OF PATIENT
26	16	B	2	187	4	150/90 130/80	No block	Spon.	Lived	Lived
27	18	W	1	156	4	160/110 130/70	Spinal	L.F.	Lived	Lived
28	17	B	1	131½	7	190/140 110/80	Caudal	C.S.	Lived	Lived
29	29	B	3	—	3	182/118 112/70	No block	Spon.	Lived	Lived
30	38	B	10	—	5	176/100 126/70	No block	Spon.	Stillb.	Lived
31	19	B	2	—	6	220/145 160/120	Caudal	Spon.	Stillb.	Lived
32	25	B	9	—	13	190/120 130/72	Cau. inser. failed	Spon.	Lived	Lived
33	33	B	4	—	5	190/125 130/80	No block	Spon.	Lived	Lived
34	14	W	1	146	3	180/100 90/70	Tuohy cat. spinal	C.S.	Lived	Lived
35	19	W	2	138	6	210/140 150/100	Tuohy cat. spinal	O.F.	Lived	Lived
36	24	W	1	210	9	216/150 140/104	Cath. caud.	C.S.	Stillb.	Lived
37	36	W	2	168	*	220/110 140/90	Caudal	Spon.	Lived	Lived
38	22	W	1	—	2	215/140 110/70	Caudal	C.S.	Lived	Lived
39	26	W	1	—	4	180/100 140/80	Caudal	Spon.	Lived	Lived
40	32	W	3	310	12	180/100 140/80	Caudal	Spon.	Lived	Lived
41	18	B	1	—	8	180/110 110/80	Caudal	Spon.	Lived	Lived
42	15	B	1	—	—	170/120 140/100	Caudal	Spon.	Lived	Lived
43	19	B	2	—	3+	220/145 160/120	Caudal	B. Hix version	Stillb.	Lived
44	14	W	1	146	3	180/100 90/70	Tuohy cat. spinal	C.S.	Lived	Lived
45	42	B	6	200	5	200/140 80/140	Caudal & spinal	Spon.	Lived	Lived
46	26	W	1	130	6	190/126 108/70	Caudal & spinal	C.S.	Lived	Lived
47	30	W	1	140	2	160/110 130/80	Tuohy spinal	L.F.	Lived	Lived
48	33	W	2	150	2	154/80 120/80	Cath. con. saddle block	L.F. & version	Lived—twins	Lived

* Unknown.

however, to maintain the sequence of the series. Some of these cases had been treated for several hours with magnesium sulfate sedation, intravenous glucose and distilled water, and oxygen. The conduction nerve block was reserved as a last resort measure. Some of

ANALGESIA—ANESTHESIA RECORD

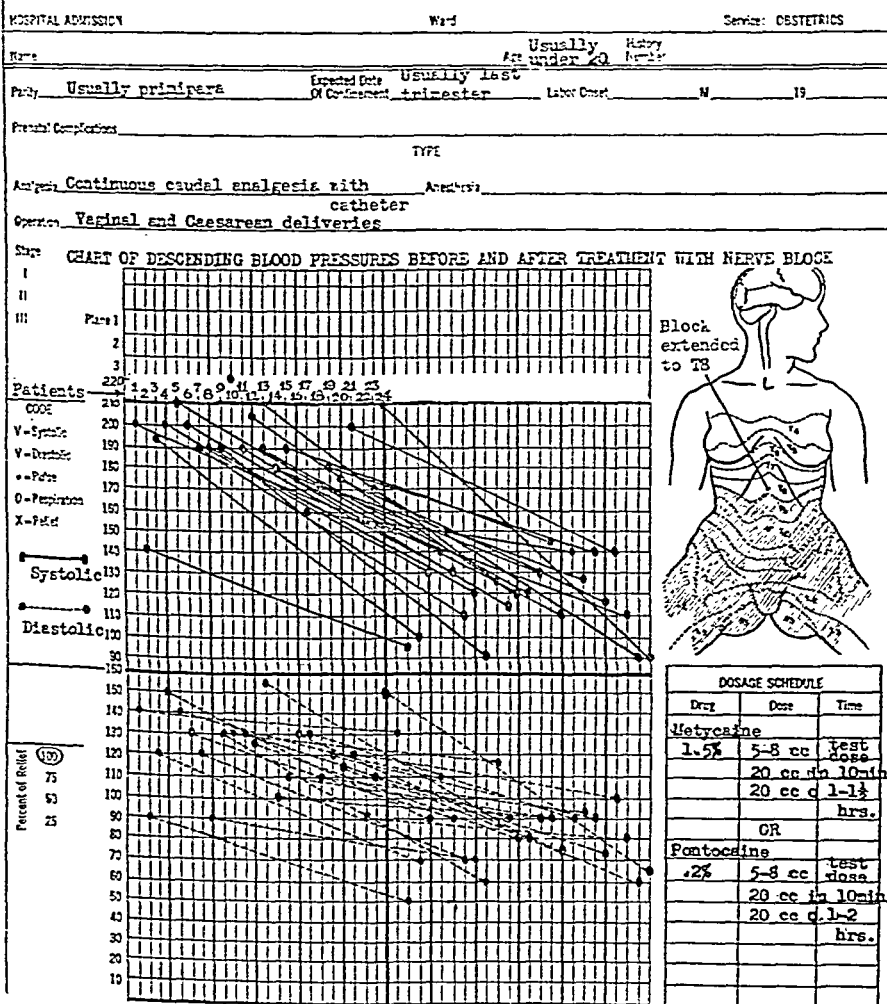


FIG. 2. THE ABOVE 24 CASES OF ECLAMPSIA MANAGED WITH CONTINUOUS CAUDAL ANALGESIA ILLUSTRATE THE BLOOD PRESSURE RESPONSES UNDER NERVE BLOCK. THERE IS USUALLY AN INCREASE IN URINARY OUTPUT

the cases were managed with conduction nerve blocks alone from the onset of symptoms for a period of from 12 to 48 hours after the last convulsion or hypertensive crisis. Only 2 of these patients had any convulsion after the institution of an effective nerve block and both of these cases had single convulsions within the first 30 minutes, which were later controlled as the nerve blocks became intensified. It is my opinion that obvious improvement resulted from the nerve blocks in all cases except in the case which succumbed imme-

3. Adequate circulating volume of fluid under filtration pressure greater than 100 millimeters of mercury systolic pressure, a wide pulse pressure, and a diastolic pressure of at least 60 millimeters of mercury pressure.

4. It has been shown that the diuretic effect of glucose administered in 20 per cent solution in distilled water in amounts individually tolerated by the patient is of definite advantage.

5. Likewise the intravenous administration of vitamins on a body requirement basis is necessary in comatose and uncooperative patients.

In eclampsia on the basis of the mechanisms described ("Control of Pain in Childbirth," Lull-Hingson, third edition), conduction nerve block of the deranged sympathetic nervous system can be established and maintained by: (a) Continuous caudal analgesia; (b) Continuous lumbar epidural analgesia; (c) Continuous spinal anesthesia. All three methods, which also provide relief of pain for labor and delivery, produce a block of the small unmyelinated sympathetic nerve fibers. With the level of block extended through the lumbar

SEASONAL VARIATION IN 48 CASES OF ECLAMPSIA

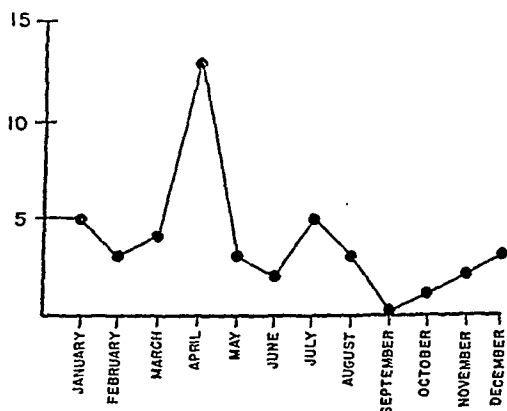


FIG. 1. THE CHOICE AND TECHNIC OF CONDUCTION ANESTHESIA IN ECLAMPSIA

plexus, a bloodless phlebotomy is produced with a vasomotor expansion of vascular bed of the pelvis and lower extremities. With the level of block extended to the eighth thoracic segment the kidneys and supra-renal glands are essentially denervated.

Since patients in eclampsia are comatose, semicomatose, irrational, uncooperative or convulsant, the ureteral or plastic catheter technics of one of the three nerve block procedures is preferred to the indwelling needle technic.

In our selection of one of the three methods we are influenced in our decision by anatomical factors which facilitate or impede a specific method. These are:

1. Palpability of the sacral hiatus or a lumbar interspinous space.
2. Disproportionate obesity or edema obscuring the sacral hiatus or lumbar interspinous space.
3. Local infection of overlying skin.

SUMMARY

Seventy-four consecutive cases of eclampsia occurring chiefly in the hospitals of Memphis, Tennessee, are presented. All of these cases were treated with conduction anesthesia nerve blocks as a measure useful in the control of the hypertensive crises attended by convulsions and nervous irritability. In 6 instances, because of edema over the vertebral column and/or uncontrolled muscular movements of patients in semicoma, these technics could not be instituted after several attempts at needle and catheter insertion. They are included,

vascular physiology superimposed on both mother and baby during the period of therapy, require an understanding that can be gained only through experience.

Physicians who are confronted with an occasional case of eclampsia without this prerequisite background will have better results in treating eclampsia with the more conservative modified method of Dieckmann.—Robert A. Hingson.)

ETIOLOGY OF ECLAMPSIA: EVALUATION OF SOME OF THE MORE RECENT THEORIES

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Texas State J. Med., 44: 527-532, (Nov.) 1948

This paper first considers briefly the eclampsia conference held under the auspices of the U. S. Department of Labor, Maternal and Child Health Division, Washington, D. C., January 27-28, 1941. It then discusses some of the more recent theories concerning the etiology of eclampsia.

At the conference the writer advanced the following theory: The element of pressure in the human female who maintains the upright position may cause such a disturbance in the utero-placental circulation as to result in degeneration of scattered areas of chorionic epithelium. From these areas of degeneration a toxin may form. Then, if the intra-ovular and intra-uterine pressure is normal, absorption by the maternal circulation may take place. If the intra-ovular and intra-uterine pressure is reduced by absorption of amniotic fluid following fetal death in utero, or by rupture of the amniotic sac, or by parturition, absorption by the maternal circulation appears to cease as the patient improves. Eclampsia is possible only in the presence of chorionic degeneration, which in turn is due to circulatory deficiency to the fetus. Toxemia of pregnancy should not be explained by a biologic concept but rather, in addition to many predisposing factors, it is more a question of evolution with failure of adaptation to the upright posture. In toxemia of pregnancy, the pressor effect of the toxin produces only hypertension. Sensitivity to this toxin produces angiospasm which is clearly seen in severe preeclampsia and must be extensive before eclampsia is possible.

An enormous amount of work has been done since the conference by Smith and Smith. According to their theory, menstruation is caused by estrogen withdrawal, and in the menstrual discharge there is a necrotizing toxin which is destructive to cells and vessel walls. In pregnancy toxemia, they have generally found an estrogen-progesterone-chorionic gonadotrophin imbalance with a notable decrease in the estrogens. With this lack of hormonal support in pregnancy, a process similar to menstruation may be inaugurated with the formation of a menstrual toxin causing in situ vessel wall, syncytial cell and decidual cell degeneration. The 2 important items lacking in the work of Smith and

diately after a spinal injection of 30 mgms. of metycaine. This patient, however, as autopsy revealed, was irretrievably damaged from interventricular hemorrhage.

ANALGESIA—ANESTHESIA RECORD

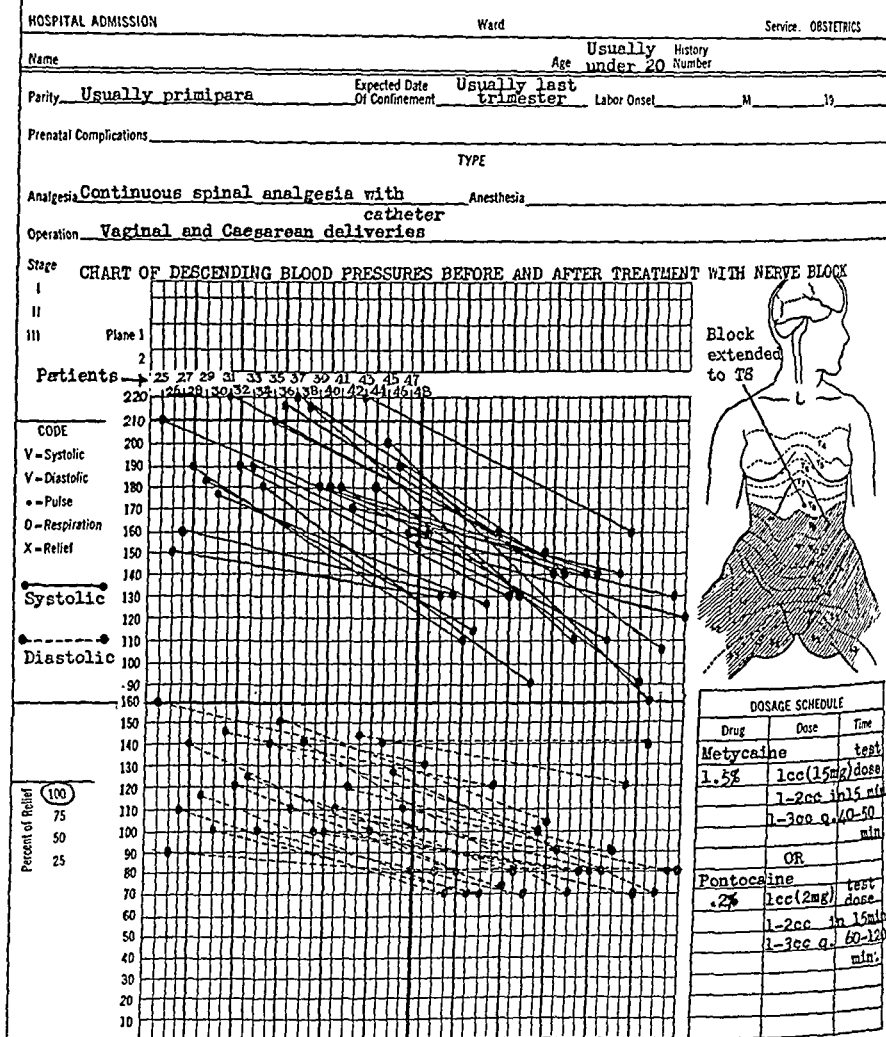


FIG. 3. THE ABOVE 24 CASES OF ECLAMPSIA MANAGED WITH CONTINUOUS SPINAL ANALGESIA ILLUSTRATE THE USUAL FALL OF BLOOD PRESSURE UNDER NERVE BLOCK. URINARY OUTPUT IS LIKEWISE INCREASED

Finally, even though the further development and standardizations of these techniques offer much in the active treatment of eclampsia, I wish to emphasize the fact that they are powerful remedies not to be used by those who have had little or no experience with them. The adjustment of individual meticulous dosage, the maintenance of slowly and evenly reduced blood pressures, the preservation of optimum circulating fluid volumes, the administration of oxygen enriched atmospheres, and the understanding of the effect of altered

that renal ischemia causes hypertension as the result of a vasopressor substance, renin, manufactured by the ischemic kidney as a compensatory mechanism to obtain more blood flow. The uterine ischemia theory of eclampsia postulates that, in a similar manner, a placental pressor substance—a protein breakdown product of syncytial degeneration—is produced as a result of faulty blood supply and that this substance causes the vasospasm and hypertension characteristic of the disease. However, at the present writing, no such placental pressor substance has been isolated and the actual mechanism by which the hypertension is caused remains unexplained.

As a corollary to this theory, Ernest W. Page believes that the liberation of thromboplastin from the ischemic placenta (along with other catabolic products of syncytial degeneration probably) plays an important role in the causation of eclampsia. Substance is lent to this viewpoint by the fact that both Copley and Schneider have identified the lethal factor of human placental extracts as thromboplastin. Copley states that the thromboplastin he obtained was a protein phospholipid fully as active as that produced by Howell from pig lungs. In vitro it causes clotting of hemophilic blood intravenously in dogs; in small doses it shortens the coagulation time, the period of higher coagulability lasting up to 2 weeks. Used locally in dog surgery, it causes almost instantaneous coagulation of bleeding surfaces (*Science* 101: 436, 1945). In Schneider's studies the placental extract was injected into the tail veins of mice. In these animals the liver appeared to be the primary site of fibrin deposition and capillary thrombosis, just as in human eclampsia (*Am. J. Physiol.* 149: 123, 1947). The production of similar lesions was effected by Dieckmann in dogs and although he called his injected material "tissue fibrinogen," it is possible in retrospect that he was dealing with tissue thromboplastin. The whole idea that some thromboplastin-like substance is active in eclampsia is not new since the concept that thrombokinase (that is thromboplastin in the presence of calcium ions) may play a role in the production of certain eclamptic lesions was discussed in 1924 by Hinselmann in his monograph and credited to Dienst. As shown by the studies of Chargaff, the placenta is the richest source of thromboplastin in the body (*J. Biol. Chem.* 161: 389, 1945). As the result of injury from ischemia and hypoxia, cytolysis of the syncytial epithelium would be expected, followed by entry of thromboplastin into the maternal circulation. This would explain the high incidence of "infarcts" in toxemic placentas and also some of the hepatic changes.

The uterine ischemic theory of eclampsia fits in well with many known facts about the disease: (1) The lower incidence in multiparae is explained on the grounds that once the uterine vessels have undergone gestational hypertrophy, they might be expected to do so again without difficulty. In the opinion of Beker, the arteries in the multiparous uterus, before as well as during pregnancy, are of distinctly larger caliber than in the primigravida uterus (*J. Obst. & Gynaec. Brit. Emp.* 55: 756, 1948). Moreover, the greater tone of the abdominal walls in primigravidae might conceivably play a role in uterine ischemia and correlate this theory with that of Paramore and Theobald. (2) The higher incidence in multiple pregnancy, twin pregnancy and hydatidiform mole becomes readily understandable as explained above. (3) The aggravation of preeclampsia in labor, as well as the increased incidence of convulsions at that time, is explained by the ischemic effect exerted by uterine contractions. (4) The increased incidence of eclampsia as pregnancy approaches term becomes readily understandable. (5) The fact that eclampsia is not known to occur in lower animals is explained on 2 grounds. In the first place, as stressed by Beker, the uterine artery in the human enters the cervix and then the main branches bend immediately upwards. They are thus working around a hairpin angle and against gravity with women in the upright position; they are hence functioning at a handicap although anastomosis with the uterine artery makes the circulation more plentiful. The erect posture may therefore be said to be a deterrent to optimal uterine circulation. (6) With the inclusion of the thromboplastin concept, the hepatic and placental lesions may possibly be explained. (7) In hypertensive toxemia of long standing the infant is often small, a circumstance which might be expected in the presence of uterine ischemia.

Smith are: (1) definite chemical determination of the substances contained, and (2) whether or not any of these substances have a pressor effect. Adhering strictly to the theory that pregnancy toxemia is caused by inadequate blood supply to the fetus, the author gives Smith and Smith credit for finding that circulatory deficiency is often the cause of pregnancy toxemia, but he suggests that hormonal imbalance or hormonal lack is an effect and not the cause.

(The uterine ischemia theory of eclampsia as described by Johnson is probably more widely held today than any other explanation. In the opinion of one of our most astute students of the toxemias, Ernest W. Page, this concept was first advanced in 1914 by James Young in his paper, "The Aetiology of Eclampsia and Albuminuria," which was published in the *Transactions of the Edinburgh Obstetrical Society*, 39: 153-202, 1914. Since that time Beker of Holland, Page, Johnson and others have assigned it a prominent place in the etiology of eclampsia.

It is common knowledge that late gestation is accompanied by an increase of approximately 1500 cc. in the total blood volume (32 per cent) as well as an increase of 1500 cc. in the cardiac output. Inasmuch as the volume of blood flowing through the kidneys, the liver, an arm, or the brain, has been shown to be the same in pregnancy as in nonpregnant women, it follows that the volume of blood flowing through the gravid uterus approximates 1½ liters per minute. In adjustment to this great increase, a parallel enlargement in the capacity of the vascular system in and around the uterus occurs as well as a doubling in the caliber of the arterial tree.

The uterine ischemia theory of eclampsia postulates that this large blood supply which the uterus in pregnancy normally receives, may become impaired as the result of a number of factors. These factors fall into 3 main groups: (1) mechanical conditions in or about the uterus militating against adequate blood flow; (2) nervous factors which influence blood flow through the autonomic nervous system; and (3) deficient adaptation of the general circulation to the requirements of the uterus in pregnancy and labor.

As examples of mechanical conditions in the uterus which may militate against satisfactory blood flow, may be cited multiple pregnancy, hydramnios and hydatidiform mole. In the first 2 of these conditions, overstretching of the uterine wall with a resultant increase in tension of its muscular lamellae may offer increased resistance to the circulation of blood within the uterine wall. The greatly increased incidence of eclampsia in twin pregnancy and in hydramnios is well established. Hydatidiform mole may result in impaired blood supply because the more rapid growth of the vesicular placenta demands a greater blood supply than does the normal placenta of the same age. The increased incidence of preeclampsia and eclampsia in hydatidiform mole, especially after the fourth month when the necessity of augmented blood supply amounts rapidly, is also well known.

Although the role played by the autonomic nervous system in vasomotor function is well known, the part it plays in the hypertension of the toxemias, if any, is not established. In the opinion of Brust, Assalli and Ferris, based on studies with tetraethylammonium chloride, the neurogenic factor is much less important than the humoral. (See next abstract.)

Deficient adaptation of the general circulation to the requirements of the uterus in pregnancy might conceivably ensue from a number of causes. In chronic hypertensive vascular disease, the generalized sclerosis of the arterioles might well hinder the vasodilatation necessary for adequate blood supply to the uterus. The fact that about a quarter of patients with chronic hypertensive vascular disease develop preeclampsia fits in well with this theory. Also in keeping with this concept is the demonstration by Priscilla White that in women with longstanding diabetes the uterine arteries are often calcified and that such diabetics are especially prone to develop preeclampsia in pregnancy. In addition, one might speculate that hormonal balance and dietary deficiencies may exert deleterious effects on the circulation and thus handicap the uterine blood flow.

But how can uterine ischemia cause hypertension and the other phenomena characteristic of preeclampsia and eclampsia? As an outcome of the studies of Goldblatt it is well known

sistently occurred in those patients who clinically were most toxic, regardless of the height of the pretest blood pressure.

These results suggest that: (1) The hypertension of toxemia of pregnancy is supported primarily by an excessive degree of humoral tone. (2) Conversely, the blood pressure in normal term pregnancy is maintained largely by neurogenic and intrinsic tone. (3) Within 48 hours postpartum of normal pregnancy there is a return to nonpregnant control mechanisms (humoral predominating). (4) Clinical assay with TEAC may be a helpful aid in diagnosis of toxemia of pregnancy and in the evaluation of changes in severity during its course.

(This valuable study was a collaborative undertaking carried out jointly by the Departments of Medicine and Obstetrics in the College of Medicine, University of Cincinnati. It is a nice illustration of the application of a relatively new method to the investigation of the toxemias and serves to remind us that as obstetricians we have much to learn from the special technics being employed today by students of hypertension in general.

There is one aspect of the authors' findings, however, which strikes me as curious. They state that the TEAC floor (depressed blood pressure levels resulting from tetraethylammonium chloride) parallels but is consistently lower than the blood pressure floor induced by high spinal anesthesia to T-3 levels. It might be expected, therefore, that spinal anesthesia in the toxemias would parallel the action of tetraethylammonium chloride and have little effect on the hypertension of preeclampsia and eclampsia. In Hingson's extensive editorial note in this issue of the Survey, P. 352, it may be seen that spinal anesthesia regularly reduced the blood pressure in eclampsia to floors as low as 90 mm. Hg. systolic and 60 diastolic. It has been my own experience with spinal anesthesia in preeclampsia and eclampsia that the blood pressure drops may be even more precipitous than those cited in the Hingson study. Moreover, Dr. Hingson tells me that in some of the eclamptics he treated the level of anesthesia did not extend above T-8 and had they all been extended to T-3, still lower floors would probably have been encountered. The mean TEAC floors reported in the above paper in eclampsia were 135/133 mm. Hg.

On the basis of this evidence it would be my reaction, therefore, that in the toxemias the TEAC floors do not parallel the floors induced in this complication by spinal anesthesia but are much higher. This observation, if it is a valid one, may itself have some bearing on the mechanism of hypertension in the toxemias and might merit further study.—Ed.)

CEREBRAL BLOOD FLOW AND METABOLISM IN NORMAL AND TOXEMIC PREGNANCY

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Am. J. M. Sc., 216: 596-597, (Nov.) 1948

Using the quantitative nitrous oxide method of Kety and Schmidt, the cerebral blood flow and related metabolic functions of the brain were studied in normal pregnant women close to term as well as in patients with toxemia of pregnancy. In comparing mean values obtained from nonpregnant individuals with those

Although the theory of uterine ischemia has much in its favor, let it be understood that it has not yet been proved. Thus, as indicated, no placental pressor substance has yet been demonstrated. The experimental evidence that constriction of the uterine arteries does cause hypertension is fragmentary and not altogether convincing as Page himself has pointed out. Moreover, why, in the light of this theory, is the incidence of eclampsia so high in certain areas, such as the southeastern states and in the Philippines? Why is it so high in nonwhites? How is salt retention explained? Valid answers to these questions may well be forthcoming in the future but meanwhile the theory, appealing though it may be, must be held sub judice.—Ed.)

EVALUATION OF NEUROGENIC AND HUMORAL FACTORS IN BLOOD PRESSURE MAINTENANCE IN NORMAL AND TOXEMIC PREGNANCY USING TETRA-ETHYL- AMMONIUM CHLORIDE

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J. Lab. & Clin. Med., **33**: 1466, (Nov.) 1948

Tetraethylammonium chloride (TEAC), administered intravenously in 400 mg. doses, induces a temporary blockade of impulse transmission at the autonomic ganglia. When neurogenic tone has been abolished in this manner, the arterioles remain responsive to humoral agents, and thus the remaining blood pressure (TEAC floor) must be maintained by humoral mechanisms together with intrinsic vascular tone.

Toxemia of pregnancy with attendant hypertension has long been regarded as a humoral disorder despite the lack of physiologic evidence. In an effort to evaluate the relative importance of humoral and neurogenic factors in the blood pressure of patients with toxemia as well as those with normal pregnancy, the authors have utilized TEAC assay to study 10 normal nonpregnant women, 10 normal term pregnancies, 18 cases of pre-eclampsia, and 5 cases of eclampsia.

In each of the normal term pregnancies, the prepartum response to autonomic block was a marked fall in blood pressure to mean levels of 55 to 65 mm. Hg. Within 24 to 48 hours postpartum, all these patients showed a striking rise in TEAC floors, the responses corresponding exactly to those of the normal nonpregnant controls.

Strikingly different responses occurred in the toxemia patients. Prepartum TEAC floors invariably remained elevated above those of nonpregnant controls and were consistently 25 to 70 mm. Hg. higher than those of normal pregnancies. With subsidence of toxemia postpartum, floors promptly fell to the normal nonpregnant range. The diastolic TEAC floor appears to be of the greatest significance in these studies, for it never fell below 80 mm. Hg. in toxemia yet was never higher than 56 mm. Hg. in normal pregnancy. The highest diastolic floors con-

OBSERVATIONS ON THE USE OF VERATRUM VIRIDE IN THE TOXEMIAS OF PREGNANCY

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M. Clinics North America 32: 1673-1682, (November) 1948

Veratrum viride was first used in the treatment of eclampsia almost a century ago. At this time there was little known of the physiology of pregnancy, much less of toxemias. Therefore little reliance can be placed in the early statistics.

In the true toxemias of pregnancy, pre-eclampsia and eclampsia, the initial sign of development is a rapid gain in weight which is the result of abnormal retention of fluid outside the vascular system. Hypertension and proteinuria are the next 2 cardinal signs of toxemia and are probably a response to an unknown physiological alteration rather than the primary lesion. Increasing edema, oliguria, hemoconcentration, the symptom of vasospasm and finally convulsions and coma follow. Improvement and recovery will only follow reversal of these pathologic changes; dehydration of the tissues and hydration of the blood must be accomplished. The control of blood pressure is of less importance than the promotion of renal function and the control of convulsions.

The beneficial effect of the fall in blood pressure brought about by the use of Veratrum viride is questionable. Veratrum viride fails in every way to aid the reversal of the fluid retention. Indeed it has been shown that in patients with this drug alone there is no increase in urinary output as long as the blood pressure remained low and that it increased when the pressure rose. Veratrum viride plays no part in increasing plasma volume.

The reduction of mortality from eclampsia reported by the older authors can be explained if one observes their whole change in method of treatment which became medical, did not make such wide use of early operative intervention and had many aspects of the modern technic of general physiological treatment.

Good results can be obtained by general measures of quiet, constant oxygen supply, urine collection and measurement by inlaying catheter and blood pressure, pulse and respiration recordings every 30 minutes. These combined with a carefully individualized plan of sedation and a reversal fluid flow caused by the administration of 1000 cc. of intravenous glucose given rapidly can control the toxemia. In the majority of instances the delivery should be accomplished vaginally and cesarean section done only on obstetrical indication.

The author concludes that effects produced by Veratrum viride are opposite those which are necessary for control of eclampsia and at this time there seems to be no indication for its use.

(Veratrum viride has never been used at the Johns Hopkins Hospital in the treatment of eclampsia and during the past decade we have depended almost altogether upon paraldehyde by rectum and intramuscular magnesium sulfate in large doses for the therapy of this disease. More recently conduction anesthesia has been employed in a very few patients.

from normal pregnant women, it was found that the latter had normal cerebral blood flow as well as comparable brain physiology, as far as most of the other cerebral functions studied were concerned. The oxygen utilization by the brain was the same in normal pregnant as in normal nonpregnant women but the volume per cent of oxygen in the arterial blood was found to be definitely lower in the pregnant individual.

Three types of toxemia were studied: toxemia superimposed upon essential hypertension, pre-eclampsia and eclampsia. In none of these was there evidence of significant deviation from normal in cerebral blood flow. However, in all there was increased cerebral vascular resistance, the greatest degree being found in eclampsia. The oxygen utilization by the brain was normal in the non-convulsive toxemias but in eclampsia this function was significantly decreased.

The older theories that there is a great reduction in the blood flow in the brain as well as deficient oxidation as the immediate cause of eclampsia must be reevaluated in the light of the present study. Inasmuch as the cerebral blood flow and the oxygen brought to the brain are normal, these postulations are not substantiated. However, the brain itself was unable to utilize oxygen to a normal extent in convulsive eclampsia.

It has been shown repeatedly that there is capillary spasm in various portions of the body during this disease. The increased cerebral vascular resistance found in all toxemias adds another reason for believing that this is a generalized vasospasm.

(Here is another splendid illustration of the application of a new quantitative technique to a fundamental problem in obstetrics. The findings have several important correlations. The fact that in pregnancy the cerebral blood flow is normal, is in keeping with the viewpoint that the blood flow to all organs with the exception of the uterus is normal in pregnancy. By the same token, the increased blood volume which is always associated with gestation must be interpreted in the light of a greatly augmented blood flow to the uterus alone. This means that the amount of blood flowing through the uterus per minute in the latter part of gestation is of the order of 1500 cc. This fact has various ramifications, one of which is its relationship to the uterine ischemia theory of eclampsia as noted in the editorial note on page 360.

The fact that the blood flow through the brain per minute in eclampsia is normal does not necessarily militate against the concept that very temporary periods of anoxia, let us say of a few seconds in duration, may not occur as the result of vasospasm. It is well known that cessation of blood supply to the kidney for exceedingly brief periods of time may raise havoc with the glomerular capillaries and the same may be true of the smaller blood vessels in the brain. The finding of increased cerebral vascular resistance in the toxemias, especially in eclampsia is most noteworthy and constitutes further evidence in view of the vasospasm basis for this disease.—Ed.)

home for further bed rest and if the loss was slight the patient was allowed up. In the more severe hemorrhages, all manipulation was avoided until the 37th week. At that time, vaginal examination was repeated after preparations had been made for cesarean section if necessary. If the placenta was palpated up to the margin or across the cervix, cesarean section was done immediately. For less severe types, the membranes were ruptured and frequently Willett's forceps were applied.

Of the 100 cases seen, it was possible to carry out a strict conservative regime in only 24 because of the period of gestation or because of previous manipulations. In the entire series, the fetal loss was 16 per cent and there were no maternal deaths. In no instance was maternal life endangered by conservative treatment. The fetal loss associated with prematurity occurred in only 6 cases, and 4 of these cases had had vaginal examinations prior to admission, which precipitated the hemorrhage. In the remaining 2 cases conservative treatment was not followed, as it was felt unlikely to be successful. Of the 11 remaining fetal deaths, 5 were felt to be due to possible mismanagement. They were due to asphyxia of the fetus because of errors in technique or because of delay in carrying out treatment. One infant died of a neonatal infection. The 5 remaining deaths were felt to be unavoidable and were due to conditions beyond the control of the obstetrician.

The author concludes that because of the patients encountered, it is usually only possible to practice conservative treatment in about 25 per cent of the cases. Conservative treatment has certain disadvantages for the mother, in that she must either be confined to a hospital or lead a very restricted life at home. However, this disadvantage seems to be outweighed by the increased possibility of obtaining a live baby. In order to carry out expectant treatment, it is necessary to have good transportation facilities, an adequate blood bank, an adequate standard of nutrition among the patients, and a resident staff experienced in its ramifications.

(This judicial appraisal of the conservative treatment of placenta previa, as it actually works out in practice, is most welcome. It has been our experience also that only about one-fourth of the cases encountered lend themselves to this type of management. Moreover, the practical difficulties of hospitalizing these patients or taking care of them at home are sometimes troublesome. Nevertheless, as the author's fetal mortality statistics attest, many babies can be saved by the employment of this program in suitable cases. It is especially reassuring to note that in this substantial series of cases there was no instance in which maternal life was endangered by conservative treatment.—Ed.)

Hence I have no brief to hold for veratrum viride and all along, like Willson, have been skeptical about its merits. Nevertheless, I can not help but be impressed by the splendid record of cases which is being built up by the Cincinnati group with the aid of this medication. I have been told informally that the series of eclamptics treated there by veratrum viride now is approaching 200 and that they have had only 3 maternal deaths. Such a record goes far to offset the bad reports circulated about veratrum viride around the turn of the century and more than counterbalances any theoretical objections to the drug which may be raised. It is hoped, however, that an extended report will soon be forthcoming from the Cincinnati group in confirmation of the hearsay statistics which I have ventured to cite.—Ed.)

THE CONSERVATIVE TREATMENT OF PLACENTA PRAEVIA

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Brit. M. J., 2: 896-899, (Nov. 20) 1948

In every discussion on the treatment of placenta previa, there are two fundamental questions to be answered, namely, what to do and when to do it. The former has fortunately been simplified with the increasing safety of lower segment cesarean section, and the procedure of choice will usually be either rupture of the membranes or abdominal delivery. However, the optimum time for this intervention is now under some question, and expectant treatment, which was previously felt to be out of the question, is gaining some advocates. Rupture of the membranes can be performed with a great deal more confidence when it has been possible to delay until the uterus is contracting and the cervix open. In addition, by a conservative approach the appalling fetal loss due to prematurity may be reduced.

Expectant treatment was first championed by Macafee and Johnson on both sides of the Atlantic. It was their contention that in the absence of vaginal manipulation the hemorrhage will never be fatal if the patient is carefully followed. By this treatment, both of these authors found a marked lowering of fetal loss. The use of cesarean section in association with conservative treatment has varied greatly in the different clinics. Subsequent reports have consistently borne out the lowering of fetal mortality by this approach to therapy, and the maternal mortality has not been increased.

The author has summarized the results obtained in 100 cases of placenta previa treated by six different physicians along conservative lines. It was agreed that no infant would be delivered before the 37th week of gestation, in so far as possible. Severe hemorrhage after the 37th week was considered cause for immediate emptying of the uterus. In those cases admitted before the 37th week with hemorrhage, they were put to bed and given sedation after the cervix had been examined by speculum. If the hemorrhage stopped, the patients were sent

injury, when the membranes ruptured. Two days later, spontaneous delivery of a normal 4-pound infant occurred. The placenta showed no abnormalities.

In summary, it may be concluded that: (1) severe injury, directly damaging the pregnancy, will produce abortion; (2) when some intrinsic pathological process is working to terminate the pregnancy subsequently, injury may accelerate it; and (3) the vast majority of injuries sustained by pregnant women produce no harmful effect whatsoever on the pregnancy or product of gestation.

Undoubtedly, surgical anesthesia and certain operative procedures occasionally initiate labor. On the other hand, the great majority of operations do not interrupt pregnancy. As a possible exception, it is well to remove ovarian tumors after the third month of gestation. Excluding infection, the essentials of good pelvic surgery on a gravid patient are careful handling of the uterus, good hemostasis, and prevention of cooling and drying of the uterine surfaces.

Various writers have pointed out a relationship between psychic shock and abortion. Although it seems theoretically possible for fear and anger to produce abortion, clinical observations offer little, if any, confirmation of this view.

The onset of signs and symptoms of abortion and premature delivery, or actual expulsion of the fetus, must follow injury within 24 hours for a causal relationship to exist. If abortion follows between 24 and 48 hours after trauma, in the author's opinion, the relation between the two is dubious, and after 48 hours it can be disregarded.

(This is a most valuable summation of a very practical subject documented by convincing statistics.)

A few years ago I analyzed a series of 53 pregnancies in illegitimately gravid white girls who stayed at our local Florence Crittenton Home during the latter half of their pregnancy. The assumption would seem justifiable that no coitus occurred in these patients throughout their stay at the Home. The incidence of premature births in this series of cases was practically the same as it was in our married white ward patients,—an observation quite in keeping with Diddle's statement that coitus has no bearing on the incidence of premature births. During the war obstetricians everywhere had extended experience with gravid wives of soldiers who followed their husbands all over the country by day coach, bus and truck. Although specific statistics on the pregnancies of these brave girls are not available, it was my own impression and that of most other obstetricians, I believe, that the incidence of abortion was not increased. Diddle's final conclusion that the vast majority of injuries sustained by pregnant women produce no harmful effects whatsoever on the pregnancy or product of gestation is in keeping with Hertig's careful observations on 1000 abortuses and is of great medicolegal significance.—Ed.)

PREGNANCY AND TUBERCULOSIS

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University of Manitoba, Winnipeg, Man.

Canad. M. A. J., 59: 462-464, (Nov.) 1948

This writer draws attention to the changing concept of the relationship of pregnancy and tuberculosis over the last 50 to 100 years. With modern methods

TRAUMA AND INTERRUPTION OF PREGNANCY

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Texas State J. Med., 44: 520-524, (Nov.) 1948

Since the relationship of various types of trauma to abortion is not well understood, a reevaluation of the subject is desirable.

For centuries there has been tacit acceptance of a cause and effect relation between coitus and abortion. Excessive sexual activity has been regarded as harmful, particularly when the menses might otherwise be expected. A. Meyer showed experimentally that repeated sexual intercourse disturbed the normal metabolic relations between corpus luteum and implanted ovum. On the contrary, Tausig, Dickinson, and Burch observed little harm from coitus in early pregnancy, but agreed that in rare instances it might produce threatened abortion. Diddle found that coitus occasionally produced threatened abortion but not premature birth. It may be safely concluded that in general sexual intercourse does not interrupt pregnancy.

Many believe that travel increases the incidence of premature delivery, yet there is no supporting clinical study. In 1944, Diddle studied 289 pregnant women who journeyed and 467 who did not. The percentage of abortions in each group was 5.6 and 17.9, respectively. Careful analysis suggested that neither the distance, method of travel, nor time of the month produced significant difference in the incidence of untimely birth.

From the standpoint of minor injuries, the airplane is safer than automobile or train. It is unlikely that retching from airsickness would induce uterine contractions. Until experimental proof is forthcoming, it seems safe to assume that the fetus will tolerate any oxygen deficit that does not seriously embarrass the mother.

It may be concluded that travel in modern conveyances seldom, if ever, initiates interruption of pregnancy unless intrinsic and extrinsic factors are already in action.

The writer describes several of the misconceptions which have been held since early times regarding the relation between injury and abortion. Cases are cited from the literature in which severe injury caused no interruption of pregnancy. In addition, the author reports 2 cases which illustrate the terrific beating a pregnant patient can take. The first patient, a 19-year-old woman, was severely beaten, choked and thrown from an automobile. Five days later she died and was examined postmortem. Many wounds and injuries were distributed over the body. The uterus, extending 3 cm. above the umbilicus, contained a normal male fetus measuring 35.2 cm. in length. There was no maceration of fetal skin and the amniotic fluid was clear. The placenta was normal. In the second case, a married woman was beaten on the abdomen by her husband in an attempt to terminate pregnancy. Scanty vaginal bleeding ensued for 12 days after the

dangerous teaching. In the first place, in my opinion, interruption after the third month is never indicated in pulmonary tuberculosis. Secondly, even if it were, I would see no reason to subject these sick women to such an extensive operation when abdominal hysterotomy would serve the same purpose. In general, the more you can stay away from major operative procedures in obstetrics and give Nature a chance, the better off the patient is. —Ed.)

ACUTE ANTERIOR POLIOMYELITIS IN PREGNANCY

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Am. J. Obst. & Gynec., 56: 143-151, 1948

In the poliomyelitis epidemic in Colorado in the summer of 1946, 900 new cases were observed and 25 cases of pregnancy with acute poliomyelitis were seen. It was found that 11 per cent of Colorado women between the ages of 17 and 40 were pregnant on any given date during the epidemic. However, 22 per cent of the poliomyelitis victims in this age group were pregnant, suggesting an increased susceptibility to the disease in pregnancy in a ratio of 2:1.

Women in all months of pregnancy were found to be equally susceptible to poliomyelitis. During the first 2 trimesters the prognosis for recovery is excellent and a study of the literature plus the present cases revealed a mortality rate of 7 per cent. On the other hand, in the last trimester the prognosis is far less favorable, with the overall mortality rate of 27 per cent, and the number of cases with residual paralysis was much higher in this group.

The hyperemia and congestion of the upper respiratory and upper digestive tracts and fatigue of pregnancy were offered as possible explanations for the increased incidence of the disease in pregnancy. However, there are probably other factors at work which are more important, but unrecognized. Estrogen and progesterone may be protective to the pregnant poliomyelitis victim early in pregnancy; however, there is no evidence of this protective action in the last trimester. It was suggested that these hormones might be so viricidal that a Herxheimer-like reaction is created in the host, causing irreversible tissue damage.

The virus apparently does not pass the placental barrier. All the children born of infected mothers during this epidemic were free of congenital disease. Poliomyelitis had no ill effect upon the progress of labor except that it necessitated an occasional forceps operation in those mothers with severe paralysis. Uterine contractions were normal. Management of pregnancy in the last trimester, when poliomyelitis supervenes, is a challenging problem. Cesarean section does not seem feasible in the acutely ill patient and delivery does not always mean the end of difficulties. The policy to follow in any given case is of necessity an individual decision.

of surgical treatment for most cases of pulmonary tuberculosis, patients can be brought through pregnancy, labor and the puerperium with the statistics for mortality and morbidity being practically no worse than those shown by female patients of similar age and similar lesions without pregnancy. In one series the mortality rate was 36 per cent in tuberculosis with pregnancy and 33 per cent in tuberculosis alone. Reactivation of the pulmonary disease is the most serious complication encountered.

The author presents several questions which are prone to arise in respect to these 2 conditions. The first of these questions is, should the arrested case, or the one who has had successful collapse therapy, be allowed to become pregnant? The author feels that such a woman can safely go through pregnancy 2 years after the arrest of the disease or, if the pregnancy occurs during collapse therapy, the pneumothorax should be continued at least one year after delivery. The second question is, should pregnancy be interrupted if tuberculosis is discovered during the first trimester? If the tuberculosis is in a treatable stage, pregnancy should not be interrupted. If the tuberculosis is very extensive and beyond treatment by collapse therapy, interruption is indicated. What is the course to follow if tuberculosis is discovered in the second or third trimester? Here, interruption is contraindicated in the great majority of cases. The patient should be hospitalized for 3 to 6 months after delivery, the pregnancy should not be allowed to go past term and lactation should not be permitted. How should labor be conducted when the patient is at, or nearly at, full term? As soon as the cervix is dilated 2 to 3 cm., scopolamine and demerol should be given. The first stage should be completed without interruption but as soon as dilatation is completed, the membranes should be ruptured and the second stage should be completed as rapidly as possible. Either local or gas oxygen anesthesia may be used. One must keep in mind the possibility of excessive postpartum bleeding which is more prone to occur in the tuberculous patient. If interruption of pregnancy is necessary in the second or third trimester, hysterectomy should be performed. In regard to the question of sterilization, if the patient is a nullipara, conservatism is the rule. However, in a patient who already has her family, sterilization is the proper approach. The prognosis for the baby is usually good. In a series of 23,000 children born to tuberculous mothers and then separated from them, only 7 developed tuberculosis.

(Because of the many social and economic factors involved, pulmonary tuberculosis complicated by pregnancy does not lend itself very well to generalizations such as the above and cases must be handled according to their individual circumstances. The trend in general is toward greater conservatism regardless of the stage of the disease, that is, toward allowing these patients to go through pregnancy provided suitable hospital therapy can be arranged.)

The advice given in the latter part of this abstract is open to question. Thus, I do not like the unqualified recommendation to rush in and deliver these patients as soon as the cervix is fully dilated. The purpose of this, of course, is to eliminate the bearing down efforts of the second stage. If the head is on the perineal floor, this advice is acceptable, but if intervention means a midforceps, the trauma which may be entailed will often offset any good which can be achieved. The recommendation that hysterectomy be performed in those cases in which interruption is indicated during the second and third trimesters, is

creased albuminuria. A premature infant was born by cesarean section, and during the operation the patient had a Stokes-Adams attack. Postpartum, the blood pressure rose, cyanosis increased and there were signs of pulmonary congestion. Edema and hepatomegaly developed. On the 23rd hospital day, she was discharged against medical advice and died 3 days later following a Stokes-Adams attack.

The writers conclude that in the absence of complications which might lead to congestive failure, the prognosis of congenital complete heart block associated with pregnancy is good.

LUTEIN CYSTS ASSOCIATED WITH HYDROPS OF THE FETUS AND THE PLACENTA

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Zentralbl. f. Gynäk. 69: 533-536, 1947

In a recent case of hydrops of the fetus and the placenta, the latter weighed 3 kilograms and had to be removed manually. Subsequently, so severe a degree of uterine atony developed that it was necessary to do a hysterectomy. At operation, both ovaries were enlarged to the size of a fist. They contained numerous multilocular cysts which were believed to be lutein cysts, and accordingly were not removed. The cysts were definitely smaller during the puerperium and eventually receded to such a size that they could no longer be felt.

The association of lutein cysts with hydrops of the fetus and the placenta may possibly be explained by the supposition that these changes in the ovary are not due to changes in the villi—as occur in mole—but rather are due to the very large number of villi. The author attempted to produce similar changes in pregnant animals by giving large doses of gonadotrophic hormone (2000 units daily).

One of the experimental animals showed an extreme overdevelopment of the syncytium with perforation of the uterine wall and hemoperitoneum. In spite of this, no lutein cysts were demonstrable in the ovaries.

Zsigmond has described another case of hydrops fetalis in which lutein cysts were demonstrable both shortly postpartum and in the course of the puerperium. Quantitative hormonal determinations were included in his study. Since that time Keuffeler and Schultheiss-Linder have described a case of hydrops of the fetus and placenta combined with lutein cysts.

The author's most recent case was that of a para 4 who had abdominal cramps at the beginning of the 7th month of pregnancy. The urine was negative, blood pressure was 115/75. On the 7th hospital day there was a marked increase in pulse rate and the appearance of a large amount of albumin in the urine. The latter contained numerous hyaline and granular casts and 5-6 red blood cells

CONGENITAL COMPLETE HEART BLOCK COMPLICATING
PREGNANCY

(A REPORT OF THREE CASES)

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J. Obst. & Gynaec. Brit. Emp., 55: 438-441, (Aug.) 1948

The first case presented in this paper is that of a 27-year-old primigravida who was seen at the 36th week of pregnancy with a bradycardia. She gave a past history of dyspnea and Stokes-Adams attacks, often being initiated by exertion. She was known to have an atrial septal defect with complete heart block. During her pregnancy, she complained of fatigue and palpitations, and so spent part of each day in bed. Examination at the time of hospitalization showed the pulse to vary between 40 and 64 beats per minute. The blood pressure was 140/70. Jugular venous pulsations were seen and were about twice as rapid as the apex beat. There was definite cardiac enlargement. A rough systolic murmur was heard with maximum intensity over the left second interspace. The electrocardiogram showed complete heart block. The patient went into labor spontaneously at term and delivered a living male infant. The postpartum course was uneventful and there was some symptomatic improvement following the birth of the child.

The second case concerns a 27-year-old primigravida, 39 weeks pregnant, who was seen because of slight edema of her ankles of 2 weeks' duration. She was noted to have a bradycardia. There was no past history of any cardiac disease. Examination showed the pulse to be 46 beats per minute, and the blood pressure was 140/74. Auscultation revealed only a basal systolic murmur. X-ray showed slight enlargement of the left ventricle. The electrocardiogram showed a complete heart block. This patient went into labor spontaneously at term, and after 15 hours delivered a normal living male infant. The postpartum course was normal and a second pregnancy was also normal. No cardiac lesion was apparent and a diagnosis of congenital heart block was made.

The third patient presented by the authors was a 28-year-old primigravida who was admitted to the hospital in the 31st week of pregnancy suffering from toxemia. She gave a past history of heart trouble since infancy and had previously been diagnosed as congenital complete heart block. She suffered from infrequent Stokes-Adams attacks. Her pulse was 39 beats per minute and the blood pressure was 170/80. She was slightly cyanotic. The heart was enlarged to the left and there was a loud systolic murmur which showed maximum intensity at the apex. There was albuminuria and a mild anemia. Electrocardiograms showed first a 4:1, and then a complete heart block. The patient's condition went gradually downhill as she developed oliguria, orthopnea and in-

rate was not significantly different in the prediabetic, diabetic and nondiabetic pregnancies. The late fetal mortality rate was 20.5 per cent as compared with other series in which the mortality in the diabetic pregnancies was as high as 50 per cent and in the nondiabetic pregnancies, 6.4 per cent. As judged from this series, it would appear that the total late fetal mortality rate commences to increase above that for nondiabetic pregnancies 15 years before the onset of diabetes and continues to increase as the onset is approached. Forty-eight patients were studied in whom diabetes did not occur until the menopause, and there were 183 pregnancies in these women before the onset of disease. In these patients the abortion rate and total late fetal mortality rate were low. It may be that diabetes after the menopause represents a different type of disease than that encountered at an earlier age.

The nature of the factor or factors responsible for the increased birth weight and the increased late fetal mortality rate in prediabetic pregnancies remains unknown. It has been suggested that the gigantism is due to elevated serum gonadotrophin and diminished serum estrogens, but the authors question this theory. They feel that an excess of anterior lobe activity, especially the diabetogenic factor, is probably responsible for the size of the fetus. Experimental evidence would also seem to indicate that excessive activity of the anterior lobe of the pituitary is responsible for the increased fetal mortality. Clinically, the injection of estrogenic substances has reduced the fetal mortality in diabetic pregnancies. It might follow that the action of such injections would be the suppression of anterior lobe activity.

THORACOPLASTY AND PREGNANCY—WITH SPECIAL REFERENCE TO CHILDBIRTH (A PRELIMINARY REPORT)

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J. Obst. & Gynaec. Brit. Emp., 55: 445-448, (Aug.) 1948

The present study includes observations on 12 patients in whom pregnancy and thoracoplasty co-existed. In all cases but one, the thoracoplasty preceded conception. The age of the patients varied from 23 to 32 years, with 7 multiparas and 5 primiparas. In one case the thoracoplasty was done when the patient was 3½ months pregnant and in the others a 2 stage, 7 rib operation had been done one to 10 years previously. Two of the patients developed slight staining of the sputum during pregnancy and one developed pleurisy 14 days prior to delivery. The average duration of labor was 15 hours and 15 minutes. Instrumental delivery was performed in 6 patients and the remainder were delivered spontaneously. Two patients developed slight dyspnea during the

per high power field. In spite of diet, progesterone, adrenal cortical hormone, atropine, subcutaneous Locke solution infusions and intravenous sugar and insulin infusions, the patient did not improve. Instead she became worse. Accordingly, artificial interruption of pregnancy was performed and hydrops of the fetus and placenta were discovered. The child, a male, weighed 1800 grams and the placenta weighed 1500 grams. Physical examination after delivery revealed that the left ovary was the size of a small orange. On the right the ovary could not be made out. On the third day of the puerperium bilateral ovarian cysts were palpable. The one on the left steadily increased in size until the 8th day and at the height of its growth was the size of two fists. The cyst on the right began to decrease in size on the 12th day and both of them began to increase on the 15th. Four weeks following delivery both ovaries were again normal in size. Thus, it is clear that lutein cysts tend to increase greatly in size during the puerperium. Hormone studies upon the urine showed that the largest quantity of pregnanediol was excreted at the time when the cysts were decreasing in size.

These investigations demonstrate that lutein cysts may occur in connection with hydrops of the fetus and placenta. They also demonstrate that lutein cysts increase in size following emptying of the uterus. Similar conditions prevail with the lutein cysts which are associated with the hydatid mole and chorion-epithelioma. The literature shows that lutein cysts associated with mole frequently develop during the puerperium.

These anomalies of the fetus and placenta are associated with hormonal dysfunction. It is not certain whether this is a derangement of the estrogenic hormone or the gonadotrophic hormone, however. It is possible that the lutein cysts may serve in part as the source of the very marked increase of gonadotrophic hormone in these cases.

PREDIABETIC PREGNANCY

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J. Obst. & Gynaec. Brit. Emp., 55: 449-454, (Aug.) 1948

For some time it has been recognized that pregnancies in women who subsequently develop diabetes mellitus are associated with high fetal mortality rates and large infants. These fetal changes become more apparent immediately before the diabetes develops but are uninfluenced by the severity of the disease. The authors have studied 43 patients who later developed diabetes in a total of 90 pregnancies.

The average birth weight of 33 infants of prediabetic mothers was 3,607 grams, while in a control group the average birth weight was 3,292 grams. The abortion

The patient was treated with small transfusions and vitamin K and the labor and puerperium were normal. The child was entirely unaffected.

THE SICKLE CELL TRAIT: INCIDENCE AND INFLUENCE IN PREGNANT COLORED WOMEN

P. K. SWITZER AND H. H. FOUCHÉ

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Am. J. M. Sc., 216: 330-332, (Sept.) 1948

Sickling of the red blood cells, a hereditary abnormality of the colored race, exists in 2 forms: (1) sicklemia, in which there is sickling of the cells but no evidence of blood destruction, and (2) sickle cell anemia, in which there is sickling with active blood destruction. The literature shows no reports on pregnancy in patients with sicklemia, but there have been several reports of patients with true sickle cell anemia associated with pregnancy. The prognosis has been observed to be poor for both mother and child. This study was undertaken to determine the incidence of the sickle cell trait in pregnant colored women, and the effects the trait might have on the course of pregnancy. Also, the writers wished to determine whether pregnancy might activate a blood destruction process in the patient with the trait.

Five hundred consecutive pregnant colored patients were examined for the sickle trait, a drop of fresh blood being examined microscopically by both of the authors. As control, 250 colored females of child-bearing age and 250 adult colored males were studied. A further group of 105 consecutive colored patients delivered in the hospital were studied for the incidence of certain obstetrical complications. It should be noted that, in general, only patients presenting some abnormality are admitted to the hospital.

The incidence of the sickle cell trait was 14.2 per cent in gravid females; 14.4 per cent in non-gravid females; and 13.2 per cent in adult males. Of the pregnant females with the trait, one was found to have mild sickle cell anemia, a ratio of 1:71.

Twenty-two of the patients with the sickle cell trait (sicklemia) were admitted to the hospital. None of the patients showed any evidence of increased blood destruction either chemically or by laboratory determinations. The fall in red blood count and hemoglobin after delivery was not abnormal.

The authors have compared the incidence of certain abnormalities found in the 22 sicklemic patients delivered in the hospital with the control group of 105 patients also delivered there and with the average reported in standard texts. They conclude that sicklemia does not interfere with normal pregnancy and delivery.

second stage of labor. No immediate postpartum complications were encountered.

The author points out that previous reports have emphasized the frequency of severe respiratory embarrassment in these patients. This was not borne out by the present series of cases. Only one instance of reactivation occurred among the 12 cases, and that was in a patient who did not carry out adequate prenatal care. Prematurity was not a major factor in these cases, and there was only one neonatal death 3 months after delivery, from gastro-enteritis. The writer concludes that in a given patient with a tuberculous lung lesion, adequately and anatomically collapsed by thoracoplasty, coexisting pregnancy need not necessarily be regarded as a severe imposition on the maternal organism.

PURPURA HAEMORRHAGICA AS A COMPLICATION OF PREGNANCY

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Brit. M. J., 2: 1020-1021, (Dec. 11) 1948

Purpura hemorrhagica is generally regarded as a rare but very grave complication of pregnancy. Reports from other clinics indicate a high maternal mortality and infant mortality. The commonest cause of death is postpartum uterine bleeding in the mother and various types of hemorrhagic manifestations in the infant. The clinical picture is usually one of numerous hemorrhages in the skin and mucous membranes during the pregnancy and, in addition, epistaxis, hemoptysis or hematuria may be present. The platelet count is often lowered and the bleeding time is prolonged. Anemia is usually present and there is often a family history of a bleeding tendency. The pregnancy and labor are usually normal; the postpartum period, however, is fraught with the dangers of hemorrhage. Treatment which is most generally advocated is the use of repeated small blood transfusions. Vitamin K may be helpful in restoring the bleeding and clotting times to normal. Interruption of pregnancy during the acute stage is contraindicated since it will merely open another channel for hemorrhage. If bleeding from the uterus is severe or prolonged, packing is indicated. The pack should be removed in 48 hours, but if bleeding recurs it should be reinserted.

Mild and transient cases of purpura occur during pregnancy, and one such case is reported in detail by the author. This patient was seen in her 35th week of pregnancy with a purpuric eruption over her face, neck and shoulders. The tourniquet test was positive, the platelet count was 40 per cent of normal, there was microscopic hematuria, and the bleeding time was prolonged. The pregnancy progressed normally and at term all evidence of purpura had disappeared.

The patient was treated with small transfusions and vitamin K and the labor and puerperium were normal. The child was entirely unaffected.

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P. K. SWITZER AND H. H. FOUCHÉ

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Twenty-two of the patients with the sickle cell trait (sicklemia) were admitted to the hospital. None of the patients showed any evidence of increased blood destruction either chemically or by laboratory determinations. The fall in red blood count and hemoglobin after delivery was not abnormal.

The authors have compared the incidence of certain abnormalities found in the 22 sicklemic patients delivered in the hospital with the control group of 105 patients also delivered there and with the average reported in standard texts. They conclude that sicklemia does not interfere with normal pregnancy and delivery.

Obstetrical histories from 56 of the sicklemic patients showed that this group had had 143 term deliveries and averaged 2.55 living children each. Histories from 200 gravid non-sicklemic women showed 478 term deliveries with an average of 2.39 living children each. The average number of abortions in the 56 sicklemic patients was 0.39 each; the average number in the 200 non-sicklemic patients was 0.40 each.

A CASE OF PROLONGED PREGNANCY

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Guy's Hosp. Gaz., 62: 299, (Nov. 6) 1948

The case is presented of a 36-year-old Danish woman who consulted the writer in July, 1947, in her second pregnancy. The first child, aged 9, had been born normally 16 days past the expected date of confinement and weighed 7½ pounds.

The menses had always been normal, occurring every 28 days. The patient kept a diary of her menstrual dates, and the last menses had been on May 5, 1947. Examination on July 26th revealed the uterus to be enlarged to the size of a 2 to 3 months' pregnancy. A very slight show, lasting 2 hours, had occurred on June 12th. Quickening took place definitely on September 17th, or 19 weeks from her last period. With these data, the expected date of confinement was fixed for about February 9, 1948. Pregnancy proceeded normally. When nothing had happened by March 5th, a trial at medical induction was made, giving 2 ounces of Oleum Ricini enemata, quinine injections, and 3 injections of Thymophysin. As a result the patient felt some vague intermittent pains for a few hours, slept well that night and returned home. On April 3rd, the membranes ruptured spontaneously early in the morning, and pains began a few hours later. At noon, the cervix admitted one finger, and by 4:30 P.M. was about three-quarters dilated. Half an ampule of Thymophysin was injected, and a boy was born at 5:15 P.M., weighing 4050 gm. (nearly 9 pounds).

Estimating the length of pregnancy from the first day of the last period, this particular pregnancy lasted 334 days, i.e., 54 days beyond the normal calculated 280 days.

(This case is of great medicolegal importance and will doubtless be cited in courts for many years to come. It is especially credible since there was no legal issue at stake and hence no reason to manipulate dates. In 1921 an English court ruled in favor of the legitimacy of a pregnancy which terminated 331 days after the departure of the husband (J. A. M. A. 77: 716, 1921) and long ago Winckel maintained that in very rare instances pregnancy may last as long as 336 days. In the United States and England there is no law with respect to the duration of pregnancy and thus individual cases are decided on their own merits. Since obstetricians are occasionally consulted by lawyers on cases involving this question, it is good to know about such examples as the above.—Ed.)

PATHOLOGY OF LABOR AND PUERPERIUM

AVULSION OF A COMPLETELY INVERTED PUERPERAL UTERUS AS A COMPLICATION OF MANUAL REMOVAL OF THE PLACENTA

REPORT OF A CASE

FRITZ WALLAU

From the University Woman's Clinic, Giessen, Germany

Zeitschr. f. Geburtsh. u. Gynäk. 128: 327-332, 1947

The patient, a 32 year old primipara, was admitted to the author's clinic on April 29, 1946. Her estimated date of confinement was the last of May, 1946. Labor began at midnight April 28, 1946 and the membranes ruptured at 7 A.M., April 29, 1946. Three hours following rupture of the membranes a living male child spontaneously delivered from occiput presentation, weighing 2300 grams. Forty-five minutes after delivery the patient was noted to be bleeding severely. The uterus was atonic and had risen high in the abdomen. Pituitary extract and ergot were given. The bleeding continued and expression of the placenta was attempted by Credé's maneuver and further pituitary extract was given. These were unavailing. The patient was then lightly anesthetized with chloroform and Credé's maneuver tried again without success. The patient was now in a state of collapse and was estimated to have lost a liter of blood. Manual removal of the placenta was attempted. When the physician removed what he thought was the placenta he discovered that he had removed the uterus and that the placenta was still attached to the lower end of the latter. The patient was then sent to the hospital.

On vaginal examination the intestine was palpable. Laparotomy was performed under ether anesthesia. The small intestine was found in the pelvis surrounded by considerable clot. It was minutely inspected and found to be uninjured. Ten cm. of the left round ligament and 6 cm. of the right round ligament could be identified. The ovaries and tubes were seized and the vessels ligated. The clot was scooped out of the pelvis. The vagina was grasped with clamps and suspended, using the round ligaments, uterosacral ligaments and right adnexal stumps. Bleeding continued from the remnants of the left parametrium, which hung in shreds of $\frac{1}{2}$ to 1 cm. in breadth. The bladder was undamaged. The vagina was closed with a single suture. The stumps were ligated in such a manner that their macerated portions could be cut away above the ligatures. The pouch of Douglas was now free of blood. The left adnexa were so badly mauled that they could not be preserved. They were removed. The vagina was drained and the operative area peritonealized by sewing the bladder peritoneum to that of the rectosigmoid. The sigmoid colon was then sutured over the area. The operative site was then washed with salt solution;

40 cc. of peritonitis serum was placed in the abdominal cavity and the latter was closed in 5 layers.

Following ligation of the vascular stumps the condition of the patient improved. The pulse remained at about 160 per minute. An intravenous infusion of Periston was given and a blood transfusion of 500 cc. with an improvement in the general condition of the patient. Every 4 hours the patient received 5 cc. of Tibatin, for a period of 4 days. She did well for the first 2 days and then developed signs of peritonitis. Despite supportive measures, the patient succumbed on the 5th postoperative day.

At autopsy the patient was found to have a thrombus in the stump of the inferior pelvic ligament on the left side. It was the opinion of the pathologist that the patient had succumbed to an overwhelming sepsis.

Examination of the uterus showed a completely inverted uterus and a portion of the vagina. After reinversion of the uterus it was found that a short piece of the vagina was adherent anteriorly and a longer one posteriorly. The one posteriorly was 10 cm. long and $\frac{1}{2}$ cm. thick and 2 cm. broad. There appeared to have been a perforation in the posterior wall of the vagina. The uterus showed the sites of avulsion of the parametrium, tubes, uteroovarian ligaments and round ligaments. The placental site was easily recognized. The reinverted uterus measured 15 cm. in length. A $7 \times 6 \times 1.5$ cm. piece of placenta was submitted with the uterus but not attached to it. Microscopic study of the placental site showed no evidence of placenta accreta. There was no evidence of placental attachment in the cervix. The placenta was not unusual microscopically. The diagnosis was puerperal uterus with complete inversion, normal placental site located near the fundus on the right hand side of the posterior wall.

The author believes that traction upon the placenta in the course of trying to remove it, plus the relaxing effect of the chloroform anesthesia, caused the uterine inversion. Then the hand of the operator must inadvertently have perforated the posterior vaginal wall and passed into the abdominal cavity. Then, mistaking the entire uterus for the placenta, the former was avulsed. Death of the patient was attributed to overwhelming sepsis.

(We plan to sell this case report either to "Believe It or Not" or "True Murder Stories," for a very substantial sum.—Ed.)

DELAYED LABOUR

R. BEARD

Adelaide, Australia

M. J. Australia, 2: 405-407, (Oct. 2) 1948

The writer considers the causes of delayed labor under 3 well-known headings: (1) the passage, (2) the forces, and (3) the passenger. With regard to the pas-

sage, dystocia arises more frequently from the soft parts than from the bony pelvis. The various pathological conditions and abnormalities that might be involved are discussed, and the importance is stressed of careful examination of the pelvis during pregnancy, in order that correct treatment at labor may be applied. A careful history, thorough clinical examination and measurement of the pelvis are essential. Pelvic radiography is advised when the pelvis is deformed or the measurements small. The author stresses the value of the pelvic classification by Caldwell and Moloy, and urges the pooling of ideas by obstetrician and radiologist. Digital examination of the pelvis is of first importance, and the value of a trial of labor should be emphasized.

In respect to the forces of labor, in spite of the importance of normal pelvic measurements, the physiologic forces of labor are the most vital factor. The factors involved in primary uterine inertia are: (1) poorly developed uterine musculature, (2) anomalies of uterine innervation, (3) loss of tone of uterine musculature, (4) mechanical interference, (5) a large fetus, and (6) fear. The great importance of fear is stressed; general management measures include reassurance and rest for the patient and reassurance for relatives. The principle of treatment of primary uterine inertia is "stimulants by day, sedatives principally at night."

With reference to the passenger, two common obstetric abnormalities which may cause delayed labor are the occipito-posterior position and breech presentation. With regard to the former, there is great divergence of opinion. The writer suggests that some overlapping factor not usually mentioned must be present, clarification of which might eliminate the disagreement. General lines of treatment are given. As to breech presentation, external version is of value as a preventive of prolonged labor.

H. W. Horn mentions the use of pituitary oxytocics. A series of 26 cases of primary uterine inertia, conducted by experts without pituitary, is compared with a series of 30 cases of inertia managed by this writer, using pituitary, usually pitocin. Comparison of the 2 series proves, first, that pituitary did not produce an increase in the fetal mortality rate, and secondly, that in no case did it produce turbulent labor, leading to maternal tragedy such as uterine rupture. It is safe to retain pituitary in the armamentarium for treatment of primary uterine inertia; occasionally it might effect a cure and often it will be of help. A patient who has been in labor for 12 hours or more, who shows mental distress, and whose pains are weak, short or infrequent, should receive $\frac{1}{4}$ grain of morphine. Persistence of inertia after rest might call for pitocin in a dosage not exceeding $\frac{1}{4}$ millilitre. If the pains are not enhanced, the dose may judiciously be repeated at half-hour intervals for 4 doses.

B. T. Mayes, in opening the discussion on this paper, emphasized the role played by fear, stating that the abolition of fear gives rise to more productive effort. His second point was the avoidance of induction of labor, especially in primiparae, particularly for what is known as post-maturity. In discussing brow presentation as a cause of delayed labor, he said that the diagnosis was seldom made until labor had been in progress for some time and the cervix was fairly well dilated. By that time the membranes had been ruptured for some

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The diagnosis of prolapse of the cord must be made early if any treatment is to be of value. The most common early symptom is slowing of the fetal heart, the cord then being discovered on vaginal examination. However, it must be remembered that in a few cases the cord will be nipped at the pelvic brim and cannot be felt by the examining finger.

The treatment of prolapsed cord depends upon the presence or absence of a fetal heart beat and on the degree of dilatation of the cervix. Early treatment is directed at relieving pressure from the cord by placing the patient in the knee-chest position or by holding back the presenting part with the fingers in the vagina. If the cervix is as much as three-quarters dilated, delivery should be carried out by forceps in a vertex presentation or manually in a breech presentation. Reposition of the cord can be attempted if the cervix is less than three-quarters dilated, but this, easy in theory, is very difficult in practice, and the actual reposition may cause further fetal distress by pressure and kinking. If reposition is carried out, the fetal heart must be carefully followed until delivery is accomplished. Internal version to a breech presentation is usually not satisfactory. Cesarean section is the method of choice when the cord is pulsating strongly and the cervix is less than three-quarters dilated. However, it is useless to subject a mother to a cesarean section if the infant is going to be stillborn.

PRIMARY POST-PARTUM HEMORRHAGE

J. B. JOYCE AND G. G. LENNON

University of Oxford, Oxford, England

Brit. M. J., 2: 740-743 (Oct. 23) 1948

During the period from 1938 to 1947, 156 cases of postpartum hemorrhage and 56 cases of manual removal of the placenta occurred in patients under charge of the Nuffield Department of Obstetrics, and the writers present an analysis of these cases.

There were 94 primiparas and 62 multiparas in this series. One hundred of the patients had a normal pregnancy in all other respects, 22 showed some form of pre-eclamptic toxemia, 4 cases had proved anemia, and in one case hydramnios was noted. Normal labor occurred in 113 cases, forceps deliveries numbered 26, other obstetrical maneuvers were performed in 16 and medical or surgical induction was undertaken in 24 cases. Multiple pregnancies numbered 3 and breech deliveries 4. Two patients had placenta previa. Hydramnios, multiple pregnancy and placenta previa did not, therefore, figure prominently in the etiology of hemorrhage in this series. The average length of labor was $21\frac{1}{2}$ hours, with extremes of $2\frac{3}{4}$ hours and 66 hours. The blood loss before and after delivery of the placenta averaged 990 cc. The placenta was delivered by fundal pressure in 105 cases, with the average duration of the third stage 30 minutes. Spontaneous delivery occurred in 27 cases, with a duration of 15 minutes. Credé's expression

hours; and version and breech extraction was to be avoided. He considered that lower segment cesarean section was the treatment of choice, together with the use of penicillin.

(As the author points out, the most common cause of prolonged labor is primary uterine inertia; and even in cases of pelvic contraction, it is often the associated inertia which impedes progress rather than diminution in pelvic capacity. Horn's discussion on the use of pituitary extract in uterine inertia is informative as is also Mayes' appropriate warning that inertia is very likely to follow induction of labor for postmaturity.

It will be noted that Horn uses the term "one-quarter milliliter of pituitary extract." This is one-quarter of a cc., or almost 4 minims. In our experience much smaller doses will prove equally effective and are presumably safer. One-half minim intramuscularly is adequate for the initial dose and if repeated every 30 minutes will usually prove efficacious. It has been our impression, moreover, that if these smaller doses are not successful, larger amounts also fail.

We are finding, as are other observers, that the intravenous drip method of administering pituitary extract for uterine inertia is safer, more efficacious and more controllable than the intramuscular technique. Here the initial dosage is one-quarter minim for the first half hour. But pituitary extract when given in the first and second stages of labor is still a threat to the safety of mother and child because it is so likely to be abused, that is, given for the sake of convenience, given in the presence of disproportion, etc. We find it necessary to use pituitary extract prior to the birth of the baby in only about 2 per cent of our labors and it is my feeling that any employment of this powerful agent which materially exceeds this frequency represents abuse and will sooner or later lead to trouble. In this connection it may be well to recall the wise counsel of Robert Gooch as stated in his "Compendium of Midwifery," published in 1849. After reviewing the many remedies advised at that time for what he calls lingering labor, Gooch writes: "My own remedy is tincture of *time*, the loss of which is the only thing to be regretted, for it at least produces no additional evils."—Ed.)

CORD COMPLICATIONS DURING PREGNANCY AND LABOUR

J. MORGAN

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Brit. M. J., 2: 820-822, (Nov. 6) 1948

It is pointed out that, considering the length and slenderness of the umbilical cord, it is surprising that cord complications do not occur more frequently. The present study, which includes 50 cases of such complications, represents an incidence of only 0.5 per cent, or 50 cases in 10,000 deliveries. The abnormalities encountered included prolapse of the cord, cord around the neck or body, a short cord, and a true knot in the cord. If the cord is around the neck, strangulation may result or, apart from causing fetal distress, the shortening of the cord which results may prevent engagement of the head and so increase the duration of labor. Cord complications are rare, but the fetal death rate due to them is quite high. In this series the fetal mortality rate was 40.5 per cent.

been located it is separated by a scratching motion of the finger tips directed toward the placenta and never toward the uterine wall. It is best, when possible, to separate it from above downward so that the uterus may contract behind the placenta and close the venous sinuses. After the placenta is separated it should be removed slowly in order to allow the remaining membranes to separate. It is necessary on some occasions to differentiate the placenta from a contraction ring, and if the ring occurs in the upper segment of the uterus only a portion of the placenta may be involved in the contraction. Here the significance of finding the fundus of the uterus before beginning the manual separation becomes apparent. In the rare case of placenta accreta, probably the best plan of treatment is to cut off the cord and wait in hope that fragmentary discharge of the placenta will take place in the ensuing weeks. 1 figure.

(The only advice given in this paper which is subject to serious question is that advanced in the last sentence. There seems to be a tendency here and there to handle placenta accreta in this conservative manner, but the complication is so rare that actual data on the results of this temporizing program are not available. The following abstract tells of a case in which noninterference with a placenta accreta yielded results which were not so good. It would be my feeling that in outright cases of complete placenta accreta (we have never seen a single case in 65,000 deliveries), the orthodox treatment by hysterectomy would certainly be best for multiparae. In primiparae also it is probably the safer program, but temporizing and antibiotics may be tried provided all concerned are prepared to face a long period of sloughing and some conceivable hazards. Case reports describing the results to be expected when a placenta accreta is allowed to slough off, would be helpful in settling this moot question.—Ed.)

REMOVAL OF PLACENTA ACCRETA AFTER ONE AND ONE-HALF YEARS' RETENTION

HANS JACOBI

Zentralbl. f. Gynäk. 70: 80-83, 1948

A 23 year old patient had had no serious previous illnesses. She had a spontaneous delivery in April, 1944. Following delivery, the placenta was retained for 9 days. Thereafter, the patient had 9 months of amenorrhea. She then had a 3 day period in December, 1944. She again became pregnant and spontaneously delivered at the end of August, 1944. (The weight of the child was not determined.) A physician could not be obtained, and the placenta was never delivered. The patient began lactating on the 2nd postpartum day and nursed her baby for 3 months. From November, 1945 until the summer of 1946 the patient had regular 3-day periods. In August, 1946 the patient began to observe more severe bleeding, and thereafter her periods lasted for 3 weeks, with considerable pain. In January, 1947 the patient observed a rise of temperature. On examination, a structure resembling the umbilical cord was noticed in the vagina. Laboratory findings revealed 60 per cent hemoglobin, 3.1 million red

was used in 23 cases with an average third stage of 70 minutes. In one case, a retained placenta was found at postmortem examination. The total number of transfusions given was 38 and the average amount of blood transfused was 2 pints. In 113 cases, an oxytocic drug was given after delivery of the placenta and in 11 cases it was given before the placenta was expelled. "Notifiable" pyrexia occurred in 17 cases, the overall puerperal morbidity being quite low. There were 2 maternal deaths, one of retained placenta and shock and the other from severe toxemia.

Of the 56 cases in which manual removal of the placenta was performed, 38 were primiparas and 18 were multiparas. Spontaneous delivery of the fetus occurred in 40 cases. "Notifiable" pyrexia was seen in 19 cases and $\frac{2}{3}$ of these occurred prior to 1942. The sulfonamides plus blood transfusions have probably been responsible for the lessened morbidity. There was no mortality in this series.

In addition to the 156 cases described, 60 cases were treated by the "Emergency Obstetric Service" for postpartum hemorrhage. One case was due to trauma, 21 cases occurred after removal of the placenta and 29 had retained placenta. Twenty-one of the last-mentioned group required manual removal, and in the remaining 8 cases the placenta was expressed. Transfusions of blood or saline were given to 49 of these patients.

The authors conclude that manual removal of the placenta is a less dangerous procedure now from the point of view of sepsis than is generally supposed. They also feel that greater use might be made of ergometrine in the control of hemorrhage and larger transfusions of blood might reduce morbidity and shorten convalescence.

A general plan of treatment for both the midwife and physician has been outlined. The management of the third stage requires above all else patience, for nature cannot be forced. If the patient's bladder is empty, the midwife should massage the fundus of the uterus in order to stimulate a contraction; separation and descent of the placenta should then occur. If it does not occur, the midwife should give 0.5 mgm. of ergometrine intramuscularly. After the placenta has been delivered, massage of the fundus should be continued so that uterine contractions will control the bleeding, and in addition another dose of ergometrine should be given. If hemorrhage is still not controlled, bimanual compression should be used as an emergency measure until medical aid arrives. The physician should be prepared to give 0.25 mgm. of ergometrine intravenously, and in 45 to 50 seconds, firm pressure on the fundus will usually suffice to deliver the placenta. However, if it is not expelled, further measures are useless immediately, as in all probability a contraction ring will be present and manual removal will probably be necessary. Following delivery of the placenta the treatment is similar to that given by the midwife.

The authors have described their method of manual removal of the placenta and have emphasized certain points. A contraction ring may be present but this can be gently stretched by insinuation of the cone-shaped hand. The cervix must always be differentiated from a contraction ring. Once the placenta has

OPERATIVE OBSTETRICS

MANAGEMENT OF OCCIPUT POSTERIOR POSITION

G. W. GUSTAFSON

Indianapolis, Indiana

J. A. M. A., 139: 280-285, (Jan. 29) 1949

In so far as management is concerned, the author has divided posterior positions into 3 categories. The first and largest group consists of those cases in which rotation occurs spontaneously after engagement. In the second group there is usually pelvic contraction or disproportion, so that even after hours of labor, engagement does not occur. The third group includes those cases in which engagement occurs but spontaneous rotation does not follow. It is in this third group that so much difference of opinion exists concerning management, and it is the group in which the author is especially interested.

Many times the posterior position occurs in borderline pelves, especially those of the android type, and because of this dystocia may be present. It has been shown to occur more frequently in the dystrophia dystocia syndrome so that often the main problem is one of evaluation of the asymmetry of the pelvis or the degree of cephalopelvic disproportion involved. Another cause which must be included is mechanical obstruction, which may prevent rotation of the head. The reported incidence of posterior position has varied from 8.1 per cent to 27.1 per cent. The incidence of persistent posterior positions has varied widely in the different clinics; however, in the present series of 2922 there were 106 such cases, or 3.6 per cent.

After the diagnosis has been made, and certainly if there is any possibility of pelvic contraction, measurements should be checked with roentgen pelvimetry. Pregnancy is apt to be prolonged; however, labor should not be mechanically induced except under special circumstances. Labor in persistent posterior position is generally slower and longer, especially in those cases in which there are firm cervixes and poor labor pains. Rupture of the bag of waters is often early. The head stays higher longer than in the anterior position, and there is less flexion. The head may enter the pelvis in either the transverse position or in one of the oblique positions and rotate posteriorly. In occipitosacral position, spontaneous delivery may occur, usually with the forehead or the base of the nose stemming under the symphysis, delivery being completed by flexion.

The posterior position should not be considered abnormal and labor should be managed as in normal presentation if the condition of the mother and baby remains good. Diagnosis of disproportion is often more difficult in this position, and unless the pelvis is highly contracted a trial of labor should be given. In following the course of labor, station correctly diagnosed is just as important as dilatation. Because of excessive moulding and long caput, it is possible

cells and 9400 white cells. The patient was hospitalized. After her temperature had been normal for 3 days vaginal examination was performed. Six cm. of umbilical cord was found in the vagina. The uterus rose to 1 hand's breadth over the symphysis. The adnexa were free.

At operation the cervix was dilated with Hegar dilators and an attempt was made to remove the placenta manually. This was not feasible; therefore the anterior vaginal vault was opened and the bladder detached from the cervix. In spite of good exposure the placenta could not be loosened. The incision was then extended toward the fundus and the back wall of the uterus was inverted. The placenta was then cut off the posterior wall of the uterus. The uterus was then reinverted and the incision closed and drained during the operation. The patient experienced some weakening of the pulse which was treated satisfactorily with adrenalin. The highest postoperative temperature was 38.4° C. The patient was up on the 10th day postoperatively and discharged from the hospital on the 16th day. Since that time she has had normal periods and physical examination recently revealed a normal uterus in good anterior position. Pathological examination of the endometrium showed a secretory endometrium with diffuse round cell infiltration and occasional hyalinized vessels; in other words, an endometritis in the secretory phase corresponding to the menstrual dates (25 days). The placenta was unsuitable for investigation after a 2 month period of fixation because of insufficient formalin in the fixing fluid. However, it was so firmly attached to the uterus that it was, in the opinion of the author, a placenta accreta.

(Am. J. Obst. & Gynec. 43: 277, 1942). This figure is in close agreement with that of Gustafson. Both Gustafson and Calkins, however, follow a conservative policy and give these patients a full 2 hours in the second stage for rotation to take place. They do so because they know that anterior rotation will ensue in almost all such cases and, on this basis, they both regard occiput posterior presentations as nothing abnormal. If this attitude were followed generally, it would reduce greatly the number of difficult forceps in these cases to the benefit of both mother and child.—Ed.)

MODERN INDICATIONS FOR CESAREAN SECTION

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Hahnemann Medical College and Hospital, Philadelphia, Pa.

Surg. Clin. North America, 28: 1487-1506, (Dec.) 1948

Now that cesarean section may be used with greater impunity, the indications have been broadened to include many conditions that formerly were forbidden because of the great risk. The choice of the type of delivery to be employed now depends entirely on which offers the least danger to the mother and child.

Fetal-pelvic disproportion at the inlet is one of the commonest indications for cesarean section. The criteria used in evaluating the contracted pelvis should include the shape of the inlet, the anteroposterior diameter or true conjugate, the transverse diameter and the size of the fetus, particularly of the head. X-ray pelvimetry and cephalometry have been of great value in determining disproportion but are not infallible and must be used only in association with other methods of clinical evaluation. The study of the problem of labor in a contracted pelvis thus depends on an evaluation of that particular baby in that particular pelvis, and such a study should be made by the obstetrician. The author emphasizes the usefulness of the Müller-Hillis maneuver in which the fetus is pushed down by a hand on the abdomen while the examining finger in the rectum or vagina determines if the head can be brought down to engagement or below. If disproportion is extreme, elective cesarean section should be selected, if moderate, the patient should be given a test of labor. The test of labor used by the author consists of good uterine contractions lasting 30 seconds or longer and occurring at least every 5 minutes. The Müller-Hillis maneuver is carried out every 3 to 4 hours and if the head cannot be brought lower on each successive attempt the test of labor is considered to have failed and section is performed.

Midpelvic contractions are a less common indication for cesarean section. Narrowing of the sacrosciatic notch to less than 2 fingerbreadths should arouse suspicion and x-ray pelvimetry should be done. A test of labor may be permitted in midplane contractions, since the head is not too low at this level to be reached by abdominal section. A contracted outlet severe enough to require section is quite rare but it must be recognized early, for once the head has reached the

for the caput to be in the mid-pelvis and with the biparietal diameter above the brim. Inaccurate diagnosis of station is probably responsible for the failure of forceps operations, which should be used only after engagement has occurred. Sedation during the first stage is imperative and the author has used meperidine hydrochloride with scopolamine. It is also felt that there should be no interference, even though progress is slow, until 2 hours after second stage pains or one hour with the head on the perineum. If progress has stopped after 2 hours of complete dilatation with the head at the midpelvis or on the perineum, the ideal treatment is manual rotation followed by forceps. If the condition of the baby demands interference early in the second stage and the head is high, version is safer than forceps with the head not engaged. If one does a version, one must always be sure that there is no obstruction and no contraction ring.

The technique of manual rotation which the author uses is as follows. Either anesthesia is used in all cases. The bladder is catheterized and a deep medio-lateral episiotomy is done. The diagnosis is then checked by the examining hand. Rotation is then carried out by grasping the occiput in the hollow of the hand and turning it through 135 degrees to come to rest under the symphysis. At the same time the head is flexed. While one hand holds the head in place, the opposite blade of the forceps is applied, and then the hand is removed and the other blade applied. Delivery is then completed exactly as in a primary anterior position. If some difficulty is encountered in maintaining the anterior position, external pressure on the forehead by an assistant will usually suffice to maintain rotation. Abdominal pressure may be used on the anterior shoulder to help rotation. If the head is displaced upwardly, as is sometimes necessary, there is always danger of prolapse of the cord.

Rotation can be accomplished by the Scanzoni or Tarnier method with the use of forceps or by the key-in-lock maneuver, and these procedures have been very successful in the hands of some obstetricians. Some men prefer to deliver part of their cases of occiput posterior as occipitosacral, especially when the head is tightly wedged in the pelvis and the pelvis is of the anthropoid type.

In the present group of 106 cases there was no maternal or fetal mortality. Six cases showed morbidity, with one case of endometritis, 2 cases of pyelitis, one cystitis, one acute suppurative pyelonephritis and one of unknown origin. In the cases of persistent nonengagement of the head, the pelvis requires careful study. A trial of labor will often be of value in determining those cases which require cesarean section. Seventeen sections were done in this series of posterior positions, but in the author's opinion these cases would have required section even if the position had been anterior. 2 figures.

(This paper, which is based upon a large personal and teaching experience, is one of the most judicious appraisals of the occiput-posterior position which has appeared. It will be noted that his series of cases posed actual problems of management, that is the occiput persisted as a posterior, in only 3.6 per cent, or once in about 28 cases of primary occiput-posterior presentations. In 780 primiparae with occiput-posterior presentations studied by Calkins, failure of rotation was observed 46 times, or in 5.9 per cent. In exactly one-half of these 46 patients spontaneous delivery took place with the occiput-posterior so that only 3.0 per cent of his series presented the problem of the persistent occiput-posterior

FETAL MORTALITY AND MORBIDITY IN CESAREAN SECTION

S. PEDVIS, J. K. L. IRWIN AND N. W. PHILPOTT

McGill University, Montreal, Quebec

Surg., Gynec. & Obst., 88: 103-107, (Jan.) 1949

This is a critical survey of fetal mortality and morbidity in cesarean section, with comparison of the results obtained under different anesthetic agents and a study of the underlying factors. Cesarean section was performed in 353 cases during the 3 periods from July 1, 1940 to Dec. 31, 1941, from July 1, 1944 to July 1, 1945, and from Jan. 1, 1946 to Dec. 31, 1946. These periods were chosen to yield sizable groups of cases operated under each of the various anesthetic agents. In this paper, infants are classified as follows: (1) normal, those perfectly well at birth who remained so until discharge; (2) morbid, those who required prolonged resuscitation or had respiratory difficulties during the first 24 to 48 hours, but who were apparently well thereafter; and (3) dead, nonviable infants, stillborn, or those who died shortly after birth.

The gross fetal mortality in the total series of 357 infants was 7.3 per cent and the morbidity was 11.2 per cent. The incidence of stillbirths and neonatal deaths was 5.3 per cent.

Prematurity, alone or in association with other causes, was responsible for 36.6 per cent of fetal deaths. Atelectasis, alone or in association with other causes, was responsible for 29.3 per cent of fetal deaths. Other causes included congenital abnormalities (12.2 per cent), deadborn, macerated (9.8 per cent), erythroblastosis (4.8 per cent), hemorrhage (4.8 per cent), and aspiration of mucous plug (2.5 per cent).

Spinal anesthesia was given in 229 cases with 184 normal fetuses, 30 morbid and 15 dead. General anesthesia was employed in 54 cases, with 41 normal fetuses, 10 morbid and 3 dead. Under local anesthesia, given in 74 cases, there were 64 normal fetuses, 2 morbid and 8 dead. From these figures it appears that general anesthesia gives a slightly higher fetal morbidity, and local anesthesia a lowered fetal morbidity but a higher mortality. However, the differences are not regarded as significant. In this series there was only one maternal death. The results for full term stillbirths and neonatal deaths were: general anesthesia, 1.9 per cent; spinal, 2.2 per cent; local, 4.1 per cent.

From a study of the type of anesthesia in relation to various indications for cesarean section, it is obvious that the higher number of toxemias and medical indications in the local group could account for part of the increased fetal mortality. However, there is a higher number of cases with placenta previa in the general group, and of Rh incompatibilities and elderly primiparae in the spinal group to account for part of their increases. When type of anesthesia in relation to fetal condition is analyzed in cases where disproportion only was the indication for section, the same general conclusions appear to hold. Disproportion was the principal indication for section.

narrowed outlet and obstruction develops, a destructive operation is the only logical treatment.

Soft tissue obstruction can occasionally be a very real indication for cesarean section. Stenosis of the cervix which may follow extensive surgical procedures or radiation therapy is often an indication for section. The same problem is presented following vaginal plastic operations and the vagina may be so rigid as to present a serious obstruction, and severe tears may result from vaginal delivery. A history of any extensive repair surgery should therefore be carefully considered in deciding upon the type of delivery to be employed. Ovarian cysts and pedunculated fibroids, if small, ordinarily cause no obstruction, but if they do take up enough space in the pelvic inlet to cause dystocia, the patient should be delivered by cesarean section.

Spastic contraction rings are quite often missed but if they are present, usually only by cesarean section can a live baby be delivered. Placenta previa and premature separation of the placenta may necessitate section if the hemorrhage is severe and the amount of cervical dilatation is small. Conservative treatment is usually not indicated except in those cases of marginal placenta previa and in premature separation when the child is dead. At one time, cesarean section was offered as a treatment for preeclampsia and eclampsia, but the results were so disastrous that it has been discarded in all modern clinics, except in the few cases in which the patient is rapidly changing from bad to worse. In uncomplicated heart disease cesarean section puts a greater strain on the heart than normal labor, so that generally speaking, heart disease alone is not an indication for section. Other conditions which may arise, such as hyperthyroidism, tuberculosis, diabetes, etc., are not indications in themselves for section, and each case must be judged individually.

Fetal indications for section include abnormal presentation and position, when this is a sign or symptom of some disproportion. Breech presentations in primigravidae should be studied closely for the same reason. Rarely, fetal monsters require section for delivery. Marked variation in the fetal heart sounds may indicate cord complications and carefully chosen cesarean sections may prove to be life-saving in such cases.

The author points out that the old dictum of "once a cesarean section always a cesarean section" is no longer necessarily true. Each case should be studied on the basis of the particular pregnancy and if there is no reason to suspect weakness of the old scar or no real indications in the present pregnancy, labor should be allowed to progress in a normal fashion.

FETAL MORTALITY AND MORBIDITY IN CESAREAN SECTION

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MISCELLANEOUS

CHILDBIRTH: DESIGN FOR THE FUTURE

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Sydney, Australia

M. J. Australia, 2: 401-404, (Oct. 2) 1948

The author considered this subject in three sections: (1) the doctor's problems; (2) the responsibility of the community; and (3) the problem of the mother. In regard to (1), apart from the regular complications of childbirth, there were some newer discoveries which would require close observation over the next decade. They were the Rh factor, diabetes and pregnancy, and rubella and pregnancy. The facilities mentioned as necessary to (2) were the provision of an efficient medical school and the provision of adequate hospitals and ancillary services. The future of the universities depended financially on government assistance and on awakening the community to the needs of a university. Discussing hospitals and ancillary services, the speaker urged the inclusion of 4 essentials: (a) provision of more beds for pregnant patients suffering from eclampsia, toxemia and chronic hypertension; (b) provision of adequate hospitals for reception and nursing of premature babies; (c) establishment of special hospitals for care and confinement of tuberculous women; and (d) setting up of a blood transfusion service. Turning to (3), the speaker said that the mother was the central figure in the design, but a shrinking figure. Decline in the birth rate was the greatest single problem in Australia. While economic conditions headed the list of reasons for restriction of families, economic remedies alone could not solve the problem.

Dr. J. W. Johnstone said that from a medical point of view, the 3 main causes of obstetric disaster and mortality were sepsis, hemorrhage and toxemia. Chemical and antibiotic therapy had radically altered the outlook on sepsis and the causes of hemorrhage were obvious. Eclampsia was still the major problem, the first difficulty being its obscurity. The basic pathological processes in the disease were: (a) a toxic spoiling going on to various degrees of tissue necrosis in patches or en masse; (b) vascular damage with thrombosis, hemorrhages and infarcts; (c) increase in the extracellular water. There was a growing belief that those processes were in large measure the result of aberrant generalized arteriolar spasm. It was necessary to be satisfied with symptomatic treatment of end results until rational specific treatment could be directed to the prime underlying cause.

Dr. Johnstone described the routine method of treatment of eclampsia at Melbourne and discussed results. Since ultraconservative elimination and the use of sedatives had been discarded, the mortality rate had dropped from 15 per cent to 10 per cent, and more recently, since the introduction of magnesium

When the effect on the fetus of the type of premedication used for the mother is evaluated, it would appear that morphine, heroin or ephedrine have an adverse effect on the fetus, but the difference was only slight.

The high fetal mortality and morbidity rates particularly due to atelectasis in cesarean section prompted special care to be given the infants after Jan., 1946. This consists of posturing the infants with head down perpendicularly for $\frac{1}{2}$ hour after birth, and at the same time excess mucus is aspirated from the mouth and pharynx. Also, oxygen is administered intermittently by mask under positive pressure. When 2 groups of infants, similar in every respect except for this special management, are compared, a trend is shown in reduction of mortality and morbidity when special care is administered.

Fifty per cent of fetal deaths occurred in association with placenta previa as the reason for section. Other indications and fetal mortality were: Rh incompatibility, 11.5 per cent; repeat section, 11.5 per cent; toxemia, 11.5 per cent; chronic nephritis, 7.7 per cent; chronic carditis, 3.9 per cent; disproportion, 3.9 per cent. The high incidence of fetal death with placenta previa emphasizes the importance of hypoxia as a result of maternal blood loss in fetal mortality.

The authors suggest that in order to reduce fetal mortality and morbidity in cesarean sections, general or spinal anesthesia without premedication but with special management of infants be utilized. With a general anesthetic when the uterus is opened the maternal respiratory system should be cleared of all anesthetic gases and 100 per cent oxygen given. When spinal is used, care should be taken to prevent wide fluctuation in the maternal blood pressure. In placenta previa blood transfusions should be given before or during operation to maintain maternal blood volume and prevent fetal hypoxia. Since prematurity is a prime factor in fetal death, cesarean section should be delayed as long as possible, consistent with the particular indication. 3 figures.

nomenon in varicose veins, it often develops in the larger vessels, greater and short saphenous and especially the ileofemoral veins and pampiniform plexus of veins in the pelvis. Three factors favor the formation of intravascular clots: factors which slow the circulation in the venous system; anything which causes increased coagulability of the blood; and changes in the intima or lining of the vessels of the venous system.

Prophylaxis against intravascular clotting of blood is the keynote of success. It must be remembered that the patient who gives a previous history of venous thrombosis is more apt to have a recurrence of the disease. The doctor must be constantly watchful for the early signs of this disease, such as cramps in the feet and legs, tenderness over the calf muscles and evidence of impaired circulation. The patient should be advised against assuming a cramped position in bed which would favor the slowing of the circulation. Early ambulation and planned exercises in bed may be of value in the prevention of clot formation.

The value of early diagnosis cannot be over-emphasized. The signs and symptoms which should be anticipated are:

(1) The complaint of a cramp in the plantar region of the foot, soreness of the heel, tightness about the ankle or stiffness or cramp in the calf muscles of the leg.

(2) Change from the usual warm dry or slightly moist skin of the feet and lower leg to a definitely cool or cold wet skin, sometimes with mottling of the skin.

(3) Definite discomfort or pain in the plantar muscles on manipulation of the foot or in the calf muscles when pressure is made on them.

(4) Homan's sign, which is elicited by forceful dorsiflexion of the foot. A positive sign is suggestive but a negative sign is not diagnostic.

(5) Palpation of the pulsation of the dorsalis pedis artery. Usually a full wave is felt, but when spasm is present it is almost imperceptible.

Active treatment is aimed at lowering the coagulability of the blood by the use of anticoagulants such as heparin and dicumarol, and maintaining adequate fluid intake so as to prevent dehydration. An attempt should be made in some cases to improve the blood flow through the vessels of the legs by parasympathetic block for unilateral conditions or continuous spinal anesthesia for bilateral conditions. A satisfactory response for these measures is subsidence of pain and tenderness and restoration of warmth and color to the involved parts. When a definite diagnosis of phlebothrombosis has been made, or if non-fatal pulmonary emboli have occurred, interruption of the continuity of the venous system at the desirable level should be carried out. It is felt by the author that this complication is of such a serious nature that the aid of medical and surgical consultants in its management is desirable from the time of its recognition.

sulfate 3 years earlier, from 10 per cent to 4 per cent. The fetal mortality had dropped from 33 per cent to 16 per cent. The main factors in the improvement were: (a) use of magnesium sulfate as a depressant; (b) depletion of fluids by intravenous administration of non-electrolytes with sodium restriction; (c) early termination of pregnancy, preferably through the natural channels; (d) prophylactic treatment by efficient antenatal care, with shifting of attention from the albumin in the urine to the earlier rise in blood pressure and the warning increase in weight. Dr. Johnstone expected that the next decade would elucidate the prime etiological cause of eclampsia.

Dr. G. Simpson said that he regretted the swing to hospital confinement; that the normal patient was safer, happier and more comfortable in her own home, and treated at much less cost. He described the visiting midwife service with its own antenatal clinics and the cooperation of the Women's Hospital for investigation and treatment of abnormalities. The majority of abnormalities were eliminated by careful antenatal care; those arising during labor were usually dealt with by transfer of patients to the hospital. Dr. Simpson strongly advocated the setting up of a "flying squad" to deal with such emergencies as those requiring blood transfusion. Turning to the modern tendency to smaller families, Dr. Simpson said that if present living standards were to be preserved, 3 or 4 child families would have to suffice, and that the political cry of "populate or perish" was unjustified. Medical men, with recent appreciation of the physiology of ovulation, were in a position to advise mothers as to how to control their fertility without mechanical or chemical aid. Finally, Dr. Simpson said that obstetricians of the past were resourceful and skillful in dealing with terrible emergencies; in the future intelligent anticipation and prophylactic measures would replace the heroic procedures of the past.

Other discussants further discussed the advantages and disadvantages of domiciliary midwifery. The advantages of nursing the baby in the mother's room were set forth. The question of whether full-time clinical chairs should be continued was discussed.

VENOUS THROMBOSIS IN OBSTETRICS AND GYNECOLOGY

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Surg. Clin. North America, 28: 1469-1476, (Dec.) 1948

Venous thrombosis has been considered a generic term which includes both phlebothrombosis and thrombophlebitis, and possibly in many instances the former represents the early stages of the process and the latter the full-blown end stage of venous thrombosis. Aside from the usual location of this phe-

separation of the placenta. Uterine inertia was the cause of hemorrhage in one case and rupture of the uterus in 2.

One hundred and eighty-six cesarean sections were done in this period with a mortality rate of 2.7 per cent. Podalic version was carried out in 186 cases with a death rate of 3.7. The mortality rates with spontaneous delivery and forceps extractions were 0.08 per cent, and 0.01 per cent, respectively.

There were 3 anesthetic deaths, 2 after ether and one following spinal. The first case died from aspiration of vomitus and the second case from massive atelectasis. The third case was a diabetic who died immediately on receiving the spinal anesthetic.

The authors have pointed out that the goal toward which the field of obstetrics must strive is the prevention of maternal mortality. However, the preventability of any one case is often difficult to establish. The death of an obstetrical patient should always raise certain questions: (1) was a diagnosis established? (2) were there adequate principles and rules for the treatment of such cases? (3) were the principles and rules carried out completely? Even though some of these are answered in the negative in a certain case it does not follow that the death was preventable, but such a group of questions will give the obstetrician insight into his own mortality statistics.

TWENTY-FIVE YEARS IN MATERNAL AND CHILD HEALTH

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Am. J. Pub. Health, 38: 1512-1520, (Nov.) 1948

Since 1913 there has been a steady decline in the infant and maternal mortality rates in Mississippi, and in the last 10 years alone the reduction in the 2 figures has been close to 50 per cent. Early efforts were directed toward better rural and municipal sanitation. Early studies indicated an incidence of hookworm of approximately 37 per cent in school children, and these studies led to the formation of a child welfare division with public health nurses to give instruction in hygiene.

The first contact of the Board of Health with midwives followed the passage of a law for the prevention of blindness. This law required that physicians and midwives be instructed in the use of silver nitrate in the newborn. In 1921, the ratio of midwives to physicians was 3:1. In that year investigation of midwives was begun and a portion of them were given permits to practice midwifery. With the aid of federal funds in 1922, a new division of maternal and infant hygiene was established. One of its earliest functions was the instruction of midwives, in the hope of reducing the appalling infant mortality rate. Syphilis was found to be a prime factor in the high stillbirth rate and the incidence of this disease among the midwives was as high as 10 per cent.

MATERNAL MORTALITY

ANALYSIS OF TEN YEAR PERIOD (1937-1946) AT THE CINCINNATI
GENERAL HOSPITAL

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West. J. Surg., 46: 611-618, (Dec.) 1948

The status of maternal mortality rates is doubly confusing because of two variables: the definition of maternal, and the factor used in calculating the mortality rate. The authors feel that all of the following should be included in maternal mortality figures: (1) deaths during pregnancy and labor, from any cause whatsoever; (2) deaths during the puerperium (6 weeks after the day of delivery); (3) deaths any time after delivery due directly to complications or sequelae of pregnancy or delivery, and continuously present since then; and (4) chorionepithelioma of uterine origin. The factors used in calculating mortality rates vary from hospital to hospital and from state to state. A plea is made for standardization of the various practices. In the Cincinnati General Hospital, the mortality rate varied between 14 and 38 per 10,000, depending on what type of deaths was included and on what group of admissions was used as a basis for comparison. A comparison was made between the statistics of this hospital and 3 other large obstetrical hospitals; however, unless one knows the basis of calculations, such comparisons are useless.

The total deaths in the 10-year period from 1937 to 1946 were 86 and the total pregnant and postpartum cases admitted were 29,193. The greatest single causes of death among patients admitted to the obstetrical service were infection and hemorrhage. Other causes included ruptured uterus, toxemia, malnutrition, hypertensive cardiovascular disease and anesthesia. The greatest causes of death among patients admitted to other than the obstetrical service were abortions and ectopic pregnancies.

Of the deaths due to infection, the cases were evenly divided between congenital and extragenital types. The extragenital infections included tuberculosis, pneumonia, emphysema, gastroenteritis, meningitis, syphilis, gluteal abscesses and septicemia. In the genital infections, 2 followed cesarean sections, 6 occurred after difficult vaginal deliveries and in 4 cases, all colored primiparas, the only explanation for the infection was that intercourse had occurred shortly before admission.

There was one death due to toxemia only; however, two of the deaths from genital infection occurred in women with toxemia. In an 18-year period, there have been 181 cases of eclampsia seen, so that the overall death rate is 1.6 per cent.

In the group of deaths due to hemorrhage, 9 cases were genital in origin and one was from spontaneous rupture of the spleen. Six cases followed premature

result are exceedingly high. Though the drug agents which are used have their own toxic effects, the morbidity of such agents is nothing when compared to that of instrumental abortions. The instruments which have been used vary from a buttonhook, through many other household articles, to the complicated system of irrigation apparatus.

Immediate death occurred in 34 per cent of the cases of death due to criminal abortion. In 62 per cent of cases death was delayed, and in 4 per cent death was only indirectly related to the abortion. Of the immediate deaths, 11 per cent were due to reflex shock. This is a vagal inhibitory reflex mechanism set in motion by external stimulation of the uterus and cervix. This reflex is usually absent or diminished under anesthesia. If this occurs, death may be instantaneous, due to sudden cardiac and respiratory arrest. Twenty-one per cent of the immediate deaths were due to air embolism which resulted from injecting air between the uterine wall and pregnancy sac under a good deal of pressure. The Higginson syringe has been incriminated in such cases. Death usually occurs about 10 minutes after injection of air into the uterine cavity. The occurrence of transient neurological signs has also been observed from sublethal air embolism. Hemorrhage is also one of the uncommon causes of immediate death.

Infection is the primary cause of delayed death and may be manifested as septicemia, pyremia, generalized peritonitis, confined local infections and toxemia and tetanus. The trauma of the operation plus the aseptic technique often employed greatly enhances the chance of infection. The gas forming bacilli and the streptococcus are the most frequent invading organisms. Distant systemic infection may occur and often a criminal abortion as the portal of entry is overlooked. The use of slippery elm or wood-wool plus the proximity of the rectum may introduce the tetanus bacillus. The organism is not rare in the normal human colon.

Continued endometrial sepsis, polypoid endometritis, tubal block and residual tubo-ovarian sclerosis are common consequences of trauma and infection and may be responsible for sterility. Abortion is also occasionally responsible for ectopic pregnancy and "pelvic invalidism."

EFFICACY OF THE SUPPOSITORY AND OF JELLY ALONE AS CONTRACEPTIVE AGENTS

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J. A. M. A., 139: 16-20, (Jan. 1) 1949

Two separate studies have been made to evaluate the efficacy of certain simple methods of contraception which do not entail the use of the diaphragm

Early emphasis was placed on nutrition in maternal and child welfare. Pellagra and dental defects were prominent among school age children. A nutritionist was added to the bureau staff to instruct the people in how and what to eat.

Through the early 1920's, rapid advances were made in the maternal and child health program. Supervision and instruction of midwives were continued at an intensive level and physicians all over the state attested to the improvement in their cleanliness and in the care which the mothers received. By 1930 the maternal and infant mortality figures had been substantially reduced, although 50 per cent of the deliveries were conducted by midwives. Also at that time, postgraduate courses in obstetrics were opened to the physicians and a full-time obstetrician went into each area to give lectures and demonstrations. Through these years the demand for antenatal care has increased and the value of anti-syphilitic treatment was recognized. Home delivery services were organized and the physician was offered the assistance of the public health nurse, plus the use of sterile ready-packed home delivery kits. However, in 1939, the leading causes of maternal mortality were toxemia and infection, both of which are in a measure preventable.

In 1943, the Mississippi Emergency Maternity and Infant Care Program was initiated and the percentage of hospital deliveries sharply increased. Planned parenthood services were also made part of the maternity service. Child guidance centers were established under the direction of a child psychiatrist and maternal tuberculosis came under closer scrutiny.

Since the war, the rate of midwife deliveries has shown gradual decline and both maternal and infant mortality have improved. There have been significant decreases in the incidence of tuberculosis and syphilis, and typhoid, malaria and pellagra are no longer problems. New obstetric hospitals are planned and child guidance and planned parenthood programs are being expanded. Hookworm and dental decay remain major problems, but in these, too, the outlook for the future is good.

DANGERS OF CRIMINAL INSTRUMENTAL ABORTIONS

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Lancet, 1: 47-48, (Jan.) 1949

The number of abortions performed in England and Wales totals between 110,000 and 150,000, and at least 40 per cent of these are induced unlawfully. There are two main classes of criminal abortion, namely, domestic, often self-induced or with the assistance of some older woman, and by the abortionists, ranging from untrained women to more skilled physicians. The mortality rate is surprisingly low (0.3 to 0.4 per cent), but the morbidity and sterility which

Gynecology

ENDOCRINOLOGY

THE VASCULAR ARCHITECTURE OF THE RAT UTERUS AS INFLUENCED BY ESTROGEN AND PROGESTERONE

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Am. J. Anat., 83: 247-308 (Sept.) 1948

The cyclic variations in the vascular architecture of the rat uterus are under the domination of the ovarian hormones. Estrogen is influential in producing early changes in the vascular pattern, including antimesometrial hyperemia, edema and mitosis. Progesterone intensifies the effect of estrogen on the blood vessels of the endometrium, particularly the "baskets" of capillaries around the uterine glands and the subepithelial plexus of capillaries, minimizes it on the capillaries of the myometrium, and augments cell division. It does, however, antagonize the effect of estrogen on water imbibition. Progesterone alone was observed not to influence the vascular architecture. In the sequence of functions, estrogen and progesterone act on the rat uterus to produce an early vasodilatation, followed by edema, and subsequently by cell division.

Material for the study of the vascular pattern of the uterus during pregnancy was obtained from (a) the sterile cornua of pregnant uteri, (b) interspaces between implantation sites in pregnant cornua, (c) implantation swellings of such cornua, (d) post-partum uteri, and (e) experimental deciduomata. Thirteen animals were unilaterally ovariectomized and 12 of these were mated and sacrificed at selected intervals during pregnancy. One animal, not mated, served as a control.

It was observed that as pregnancy progressed the extra-uterine plexus of vessels from the uterine artery and vein of both the sterile and the pregnant cornu of the uterus increased in size. However, the vessels of the pregnant horn developed to a greater extent and were more slowly perfused with saline than those vessels of the plexus of the sterile horn.

In the sterile cornu and between swellings of the pregnant cornu, variations in the vascular pattern were similar, although a lag phase was apparent in some of the non-pregnant specimens. The localized antimesometrial hyperemia was observed on day 6 and day 7 but was not apparent at a later time in the pregnant cycle. At this stage, some 6 days after fertilization, implantation takes place. That antimesometrial hyperemia is not a response to the presence of the blastocyst is shown by its occurrence in the sterile cornu. In cytological studies of the decidual reaction in the rat during early pregnancy, Krehbiel ('37) observed that

—one in Baltimore and the other in Columbia, S. C., and vicinity. The contraceptive agents, with instructions for their use, were supplied to women who were followed for certain lengths of time. In both studies, a preliminary trial period served to eliminate those women who were not interested in the method and who might have been pregnant at the time the agents were supplied.

In Baltimore 333 women, who used a suppository containing phenylmercuric acetate as the only contraceptive agent, were followed for intervals which ranged between 6 and 28 months. The total period of exposure to pregnancy of these women while under observation was 4,210 woman-months. Fifty-seven conceptions took place, or 16.2 per hundred woman-years of exposure. In 18 of these 57 cases the woman acknowledged failure to use the suppositories on one or more occasions. Subtracting these, there were 39 conceptions which occurred despite the regular use of the suppositories, or 11.1 per hundred woman-years of exposure.

In the South Carolina study various types of simple contraceptives were used, including jelly alone, cream alone, suppositories, and sponge and foam powder. Fifteen hundred and seventy-three women were followed for intervals which ranged from 12 to 37 months. The total period of exposure to pregnancy of these women while under observation was 21,088 patient-months. Seventy-nine pregnancies occurred despite the regular use of the contraceptive agent, giving an over-all figure for the non-diaphragm methods of 4.5 conceptions per hundred woman-years of exposure.

The efficacy of the diaphragm and jelly in New York has been reported by Stix and Notestein as low as 12 conceptions per hundred woman-years of exposure, and in other cities of the United States from 15 to 18. On the other hand, in San Juan, Puerto Rico, the identical method has yielded a figure of 33. This shows clearly that the end results of any birth control program will depend more on personal factors (such as earnest desire to prevent conception and intelligence) than on the inherent efficacy of the procedure employed. The divergence of the figures reported in the present study doubtless reflects the same circumstance. Moreover, the sources of error in calculating results are many, and, all in all, statistics on the intrinsic value of any given method must be regarded as approximations only. Although the present study is vulnerable to all these criticisms, it at least raises the question as to whether the superior efficacy of the diaphragm over other procedures has not been greatly exaggerated. It may be that certain women, highly skilled in the insertion of the diaphragm, will receive better protection from that technic, but surely mass studies on the diaphragm have not shown greater efficacy than is reported in this paper by simpler procedures. Hence, the conclusion is made by the writers that these latter methods—especially the suppository, the simplest of them all—deserve more widespread trial than they have heretofore received.

URINARY EXCRETION OF OESTROGENIC SUBSTANCES AND 17-KETOSTEROIDS IN CASES OF METROPATHIA HAEMORRHAGICA

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Acta endocrinol., 1: 189-201, 1948

The total urinary output from 15 patients suffering from metropathia hemorrhagica was collected daily. The excretion of estrogenic substances and of 17-ketosteroids was determined in these samples of urine. The method used was the same as in a similar investigation on 19 healthy women. All the present 15 patients exhibited the classical picture of metropathia hemorrhagica.

The material is divided into 3 groups: Group 1 includes the patients treated with curettage only; Group 2 patients were treated with implantation of omental flaps in both ovaries; and those in Group 3 were given treatment with prominal, 1 gm. 3 times daily, for about a week. The excretion of estrogenic substances was considerably higher than normal in all the cases, and no decrease could be observed during the bleeding periods. Following omental implantation, the estrogenic excretion ceased and then increased after varying periods of time. Estrogenic excretion also ceased during treatment with prominal, but returned to the premedication level a few days after completion of the treatment.

The estrogenic excretion appears to increase with the duration of the disease.

The excretion of 17-ketosteroids was considerably lower than in healthy women. Neither omental implantation nor prominal treatment had any effect on this excretion.

The pathogenesis of metropathia hemorrhagica is discussed in light of the results of this study. An experimental investigation on guinea pigs has been instituted in order to discover which structures in the ovary are responsible for the increase in estrogenic excretion. 6 figures.

(Interesting as this study is, it throws no conclusive light on the hormone mechanism of metropathia hemorrhagica. While various concepts are cited, one gets the impression that the author is partial to that of Westmann (Geburtsh. u. Frauenheilk. 5: 415, 1943), that the chief factor is a disturbance in gonadotrophic production as a result of an increased hypothalamico-hypophyseal function. This is apparently the basis for her employment of prominal in one group of experiments. While its chemical nature is not stated, it was apparently suggested by Westmann for the suppression of the assumed overactivity of the hypothalamus. Certainly these premises cannot be accepted without question. The group of experiments in patients treated with omental implantation in the ovaries must likewise be looked upon with some doubt. This operative procedure, which I do not believe is known in our own country, the author likewise attributes to Westmann (Gynecologia 122: 220, 1946), with the explanation that this operation permits estrogenic substances to be carried by the portal blood stream to the liver, where they are partly inactivated.—Ed.)

at the sixth day the implantation zone was differentiated only by the presence of prominent capillaries. The importance of the vascular system in determining the site of implantation has been suggested in the human and in other mammalian uteri.

After the ninth day of pregnancy, changes in the vascular pattern were limited to studies of sections obtained from the sterile cornu, and up to the tenth or twelfth day there was no essential difference between the state of blood vessels of the empty cornu in pregnancy and pseudopregnancy. There were the same subepithelial vessels and the prominent capillary supply of the growing uterine glands. On the fourteenth day the generalized vasodilatation throughout the section was of special interest, since at this time blood appears on the vaginal mucosa—the “placental sign” of Long and Evans ('22). However, in the present specimens there was blood in the lumen of the uterus long before it appeared as the placental sign in the vagina.

Another outstanding change in the vascular pattern of the sterile cornu of the rat was the appearance of edema, observed on the sixteenth and eighteenth days. By the eighteenth day, the uterus is approximately doubled in size. The decreased vascular population which is concomitant with an increase in size is similar to the effect of estrogen injected into rabbits, as observed by Fagin and Reynolds ('36).

The typically distended estrous uterus was observed 24 hours, and its subsequent collapse 30 hours, after parturition. Ovulation is known to occur in the rat shortly after parturition.

The present study corroborates other observations, that the experimental deciduomata are in all essentials like those produced in the normal course of early implantation of the embryo. This conclusion is based on the characteristics of the vascular supply to the 2 regions of the deciduoma, namely, the antimesometrial or lipoid moiety of Krehbiel and the glycogen-bearing mesometrial portion with its wide blood sinuses, since both regions are present in the experimentally produced deciduomata exactly as in the pregnant state. 47 figures.

(The vascular mechanisms of the uterus which are concerned in the reproductive phenomena have been extensively studied since the epoch-making contribution of Markee in 1940, based on a study of endometrial implants in the anterior eye chamber of experimental animals. Since menstruation is, after all, a vascular phenomenon, and since almost nothing had previously been known about the vascular behavior, the importance of such studies is evident. However, there is still much to be learned in this field, such as the exact relation of the ovarian hormones to these vascular processes, and the study of Williams is a contribution along this line, although she has not utilized Markee's technique in her investigations. In some of the problems she has discussed, it would scarcely be applicable. A recent point of confusion has arisen in the fact that in certain types of monkey there are no coiled arterioles whatever in the endometria, and yet menstrual bleeding may occur, though usually very scanty. No satisfactory explanation, so far as I know, has as yet been offered for this fact.—Ed.)

will clear up with the discontinuance of the medication. In those remaining, a diagnostic curettage can rule out malignancy.

Most of the symptoms of menopause are caused by the surplus of gonadotrophic stimulating hormones due to the withdrawal of the estrogenic hormones. It is thought that this hyperactive pituitarism combined with hyperadrenalism will ultimately stabilize the endocrine system. The long use of estrogen will retard this adjustment.

Another danger is addiction. The patient becomes shot or pill conscious. This is particularly dangerous where hormonal preparations can be purchased without prescription. The great expense to the patient is another consideration. Too often routine estrogen therapy leads to the ignorance of serious symptoms developing during the period.

A systemic approach to the menopause should be adopted. A thorough psychiatric work-up is of great importance at this time. A careful examination should be made and any patient with a family history of, or who has had any type of malignancy, menorrhagia or metrorrhagia, should be placed in the group of those where estrogens are contraindicated.

There are a number of drugs that may be substituted. Synthetic vitamin E such as ephynal acetate has been used by the author with splendid results and no after-effects. The use of the male sex hormone is rational therapy since its action is inhibiting to the pituitary gonadotrophic activity and given in small doses does not produce side effects of masculinization.

Estrogens can be given without danger when indicated if given for a short time and in small doses. The patient should be seen every 3 weeks and therapy re-evaluated. The author feels that the vitamin B complex should always be given to any patient receiving any type of estrogenic substance.

(The author's warning against the injudicious over-use of estrogenic hormones may be heartily endorsed, though not particularly on the basis of the still unsubstantiated theories advanced by Ayre. One of the hazards of such therapeutic abuse of the estrogens is that of producing postmenopausal bleeding. Even in the early days of stilbestrol therapy, this undesirable sequel soon became apparent, and I myself encountered so many cases that I was moved to publish a paper in the *Journal of the American Medical Association* warning against excessive or prolonged estrogen therapy of this sort, and reporting a group of cases of postmenopausal bleeding thus produced. Other authors have repeated these warnings since then, but the abuse is still a prevalent one, as every gynecologist knows. The way of the reformer is indeed a hard and discouraging one. It is surprising how many doctors still prescribe estrogens, especially of the oral group, to patients without the slightest restrictions as to the duration of such therapy. In a large proportion of such cases no estrogen therapy at all is necessary, but in the minority of cases in which it is indicated, it should be used only when and if vasomotor symptoms are troublesome, and never continuously.

I have never written a prescription for an oral estrogen without some such directions to the patient as "One tablet nightly, only when and if flushes are troublesome." Incidentally, in these days of potent oral estrogens, there is no advantage and much disadvantage in the "needle" methods of menopausal women. I do not believe I have for many years given a single "shot" in cases of this group, so that it is obvious that I endorse the author's views on this subject. However, I do not know that I take as seriously as he does the theory advanced by Ayre as to the local fixation of estrogens, nor do I value as highly as he does the virtues of vitamin E and vitamin B in this field of organotherapy.—Ed.)

THE URINARY EXCRETION OF 17-KETOSTEROIDS IN WOMEN
DETERMINED BY THE ZIMMERMANN REACTION

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*Department of Women's Diseases, Karolinska Sjukhuset, Stockholm, Sweden**Acta endocrinol., 1: 238-247, 1948*

The Zimmermann reaction was found to give approximately the same results as other methods of determining the 17-ketosteroid excretion in the urine reported in the literature. In a series of 19 healthy women studied for at least one ovarian cycle, the urinary output of 17-ketosteroids was found to vary between 1 and 16 mg. per 24 hours. Most of the levels were between 4 and 8 mg. (170 of 279 determinations). There seemed to be a tendency toward higher levels during the secretory phase. Of 29 cases of virilism, 3 with strongly pronounced virile symptoms showed an increased urinary excretion of 17-ketosteroids. Three of 6 cases of Cushing's syndrome showed an increased 17-ketosteroid level. 1 figure.

INDISCRIMINATE USE OF ESTROGENS IN THE MENOPAUSE

J. M. HABEL

*Suffolk, Va.**Virginia M. Monthly, 2: 517-520, (Oct.) 1948*

The increasing number of patients seen with uterine bleeding due to overstimulation of estrogenic hormones and a recent article by Ayre showing a definite relationship between nutritional deficiency, excessive estrogens and inflammation as a possible cause of carcinoma of the cervix make it necessary to examine the excessive use of estrogens.

It is important to realize that few women going through the menopause need much therapy. However, it is far easier for the physician to ascribe all symptoms to the menopause and turn the patient over to a nurse for a number of estrogen injections than to evaluate the case. Another reason for such a procedure by the physician is a financial one. Most typically menopausal patients are better treated with mild sedation and a little psychotherapy.

The results of excessive estrogens can be very damaging. That there is a relationship between excessive estrogens and a predisposition to carcinoma is becoming increasingly more certain. Ayre states, "estrogen fixation and concentration in infected cervical tissues is believed to be a gross stimulating factor pre-disposing to cancer."

Also excessive use of estrogens may produce excessive bleeding. Most of these

THE MENSTRUAL CYCLE

HISTOLOGICAL STUDIES IN AMENORRHEAS TREATED WITH PROGESTERONE AND PARASYMPATHETICOMIMETIC SUBSTANCES

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From The University Woman's Clinic of Würzburg, Germany

Geburtsh. u. Frauenhk. 8: 576-584, Aug. 1948

In the study of amenorrhea today a combination of factors is recognized as responsible for the syndrome. Both the endocrine and the neurovegetative systems are involved.

Numerous investigators have treated amenorrhea with parasympatheticomimetic materials (Prostigmine, Pilocarpine and Moryl). On the other hand, others have employed progesterone.

The value of any such treatment can only be assessed by the histologic study of the mucosal response to these drugs.

Five patients who had had periods of amenorrhea ranging from 4 months to 4 years, received .00025 grams of Moryl subcutaneously on each of 5 consecutive days. Following the treatment only one of the cases showed any bleeding. Study of the endometrium in this case showed an atrophic pattern before treatment and a very slight degree of proliferation following treatment. The bleeding was believed to have been due to diapedesis associated with the well-known vascular dilatory action of parasympatheticomimetic materials. The slight degree of endometrial proliferation would appear to support the view that the parasympathetic tends to stimulate follicle ripening.

Six cases were treated with Prostigmine. On 5 consecutive days they received respectively doses of .0005, .0005, .00075, .001 and .001 grams subcutaneously. Bleeding occurred in 2 of these cases. In the 1 an increase in the proliferative pattern of the endometrium was observed throughout the treatment. In the other a secretory pattern was manifest throughout. This second case may be characterized as true menstruation: but bleeding in this case might well have occurred without the Prostigmine because the secretory pattern was already present.

Fifteen cases were treated with Progesterone. Each of these received .01 grams of Progesterone on 5 consecutive days. In 10 cases bleeding was produced. In these cases 2 mucosal patterns occurred. In the first the mucosa was transformed either from a slightly or markedly proliferative pattern to a slightly or markedly secretory pattern. On the other hand, if the pattern was markedly proliferative or markedly secretory before treatment, desquamation occurred. Thus, in 7 cases the bleeding was the result of diapedesis. In only 3 cases did menstruation occur. Burger thus concludes that Progesterone produces true menstruation only in those cases in which the mucosa at the beginning of the experiment is either markedly proliferative or secretory.

ARE ESTROGENS CARCINOGENIC IN THE HUMAN FEMALE?

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Ann. West. M. & S., 2: 334-336, (July) 1948

Attention is called again to the dangers of indiscriminate use of estrogens. Harrel has stated that he has never seen an endometrial carcinoma in a previously oophorectomized patient; this is corroborative evidence of the stimulating effect of estrin on the endometrium.

Hyperplasia of the endometrium persisting after the menopause apparently predisposes to carcinoma. The only known cause of endometrial hyperplasia is hyperestrinism.

The common co-association of uterine fibroids with endometrial carcinoma is significant since the level of estrogenic stimulation may be higher in this group than in the case of the non-fibroid uterus.

Ayre and Bauld found that high activity of endogenous estrogen and a deficiency of vitamin B complex was present in the majority of 15 cases of carcinoma of the uterus. In a study of 55 estrogen-producing tumors of the ovary at the Mayo Clinic, the incidence of endometrial carcinoma was 27.3 per cent.

The author advocates the cautious use of estrogen with frequent rest periods.

(The question of the possible carcinogenic hazard of estrogen therapy has been discussed so many times in these columns that it need not be again elaborated upon. In so far as the human female is concerned, there are only a few reported cases in which carcinoma of the breast or endometrium has occurred in women following estrogen therapy. Since innumerable cases have received even excessive therapy without this sequel, and since innumerable women have died of cancer without having received estrogen therapy, the post hoc propter hoc factor cannot be eliminated in the consideration of the few reported cases mentioned. It is generally agreed, however, that in experimental animals the estrogens are of some importance in the incitation of cancer in those organs and tissues normally under the physiological domination of estrogen, meaning the genital tract and breast. Cancer-like lesions have been produced by numerous workers in both the breast and uterus, but as a rule these lesions regress after withdrawal of the hormone, so that they are not genuinely neoplastic. So far as I know, in only one animal, the mouse, has genuine cancer been produced by estrogens, these observations being reported by Gardner and his associates at Yale.

There is considerable evidence, only part of which has been mentioned by the author, to suggest a predisposing role of estrogens in human cancer, and a possible hazard in their use in patients with so-called precancerous lesions, those with a strong hereditary history of cancer, or those who have actually had operation or radiotherapy for cancer. The wise clinician will certainly wish to go easy with estrogens in such cases, or avoid their use altogether.

The author's comment as to the possibly high level of estrogens in women with myomas is not supported by any evidence that I know of, and the work of Ayre and Bauld, to which he appears to attach significance, is still unsubstantiated.—Ed.)

answer is accepted. One theory that needs to be pursued further is the work by Rona and Waldbauer on the retardation or prevention of gelation by changes in the colloid system brought about by cytolysis *in utero*.

(The question of why menstrual blood does not coagulate has been discussed for a great many years, and in spite of provocative studies of recent years, one cannot be altogether sure that it has been satisfactorily solved. For many years the explanations offered revolved about a biochemical change produced in the blood during its passage through the uterine wall. One group believed that anticoagulation factors were added, the other that the clotting principles were in some way abolished. During the past few years a number of authors have made out a pretty good case for the view that menstrual blood really does clot within the uterus, but that the clot is as a rule dissolved in utero by the action of certain fibrinolytic enzymes. It is quite possible that this will prove to be the correct explanation, but it is perhaps wise to keep an open mind for a while longer. That some of the proponents of this newer view consider the question completely closed was indicated to me when I got a rather indignant letter from one of them simply because in my own textbook I had not more emphatically expressed complete acceptance of the newer view, although I set it forth fairly enough. In the paper abstracted here, Pierce indicates an equally open mind, so he may also get a little fan-mail on the subject.)

Many women, and probably some physicians, attach too much importance to the clotting of menstrual blood which so many patients have. While it is in a general way true that menstrual blood does not clot, there are many exceptions in essentially normal women. Whatever the underlying explanation may be, there is no doubt that women with normally rather profuse flow, as well as those with pathologically free bleeding, often show various degrees of clotting. In itself the clotting has little significance other than it is apt to accompany profuseness of flow. It is rare to find clotting in the case of women with scanty flows. When clots are large they can produce rather colicky uterine contraction pains, and may of course be a source of discomfort and embarrassment to the patient. A favorite comparison among such women themselves, in describing their embarrassment at the flopping escape of large clots, is with the cows in the pasture.—Ed.)

Thus, bleeding may be produced either by the exhibition of parasympatheticomimetic materials or with Progesterone. In the latter case the treatment is more often successful in producing bleeding. No bleeding whatever was produced in primary amenorrhea or those cases of secondary amenorrhea in which the endometrium was absolutely atrophic prior to treatment.

Burger concludes as the result of this study that it is impossible to treat amenorrhea properly either with parasympatheticomimetic drugs or with Progesterone. However, bleeding which may be produced by these means may have a favorable psychic effect on the patient.

(The smallness of the authors' series gives it little statistical value, but the conclusions which they reach are pretty much those which have been distilled from the observations of a great many other investigators. I do not know just what "Moryl" is, but I gather that it is one of the so-called parasympatheticomimetic group, to which prostigmine belongs. It is not surprising, therefore, that it produced little or no proliferative effect upon the endometrium. As a matter of fact, in only 1 of the 5 patients in which it was used was bleeding noted. If this were the limited end-object of treatment, certainly far better results can be obtained by adequate administration of such estrogens as diethylstilbestrol. The bleeding results after progesterone were definitely better, and in at least 3 of the 15 cases menstruation was presumably initiated. Here again I believe that estrogen therapy might have given comparable results, certainly in so far as the production of bleeding is concerned. I agree with Burger as to the favorable psychological effects often justifying such therapy, with full appreciation of its limitations, and with also full appreciation of the harmlessness of amenorrhea per se. It should be added, however, that some excellent gynecologists appear to be partial to the progesterone plan, and believe it not infrequently is followed by an inauguration of the normal function.—Ed.)

THE COAGULABILITY OF MENSTRUAL FLUID

L. C. PIERCE

J. Bowman Gray School Med., 6: 158-161, (Sept.) 1948

The writer presents a review of the recent literature on the coagulability of menstrual fluid. From the evidence found, it is believed that noncoagulability of the fluid is normal.

Several of the theories to explain this belief are presented. Although it has been found that there is a decreased amount of thrombin in the systemic circulation during menstruation, the decrease is not enough to interfere with coagulation, and lack of clotting is most likely due to a local process. Certainly, the exact mechanism of this noncoagulability has not been definitely determined, but it seems logical to assume that it might be due to a combination of factors. The experiments of Schickele and King for an anticoagulant cannot be discarded. On the other hand, it is difficult to disprove the presence of a lytic agent. The latter could conceivably lyse any clots that formed due to an insufficient elaboration of the anticoagulant. More work needs to be done on this subject before a definite

inguinal region was present. Examination under anesthesia showed normal labia, clitoris and urethra, but complete absence of vagina and apparent absence of uterus and ovaries.

A new vagina was constructed by McIndoe's method. A globoid mass was palpated in both inguinal regions and further congenital abnormality in the ovarian position was suspected.

At operation the hernial sac was opened and revealed a normal ovary, Fallopian tube and a rudimentary uterus on the posterior wall fading away into the neck of the sac. The contents of the sac were returned to the abdomen and repair was completed. A similar abnormality on the opposite side was dealt with in a like manner. Convalescence was normal.

It was assumed that there had been failure in the development and fusion of the Mullerian ducts resulting in the absence of the vagina and in the uterus represented by plaques of uncanalized uterine muscles. The ovaries probably descended into the inguinal region from the lumbar region about the 8th week. 1 figure.

(Combinations of congenital anomalies are quite common and this fact should be borne in mind when patients present themselves with such anomalies as congenital absence of the uterus and vagina. It is a well-known fact that many such patients also have associated anomalies of the urinary tract, such as unilateral absence of the kidney, horse-shoe kidney, ectopic kidney, double kidney pelvis or double ureter. An intravenous pyelogram should constitute a part of the examination of such patients. Hernial sacs in such cases may contain the gonads, as in the case reported by the author.

In a large proportion of cases designated as congenital absence of the uterus, the organ is not really completely absent but exceedingly rudimentary, often being palpable as a tiny, almost imperceptible nubbin. Such very rudimentary uteri are often of unfused type, laparotomy showing a tiny nubbin well to each side of the midline. Usually these nodules on microscopic examination show at least a small amount of endometrium, the picture sometimes resembling that seen with an adenomyoma.—Ed.)

ACUTE NON-VENEREAL GENITAL ULCERS IN WOMEN

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Zeitsch. f. Geburtsh. u. Gynäk. 128: 307-326, 1947

Lipschütz and others have described a type of acute non-venereal vulvar ulcer (*Ulcus vulvae acutum*). This has been attributed to *bacillus crassus*. It has been described as occurring predominantly in young girls of 14 to 20 years. Seventy per cent of the cases have been virgins. The eldest patient was 69 years of age and the youngest 3 years. In most cases the ulcer is located on the inner aspect of the labia minora, but sometimes occurs also on the labia majora, in-

VULVA AND VAGINA

REPORT OF FOUR CASES OF GRANULOMA INGUINALE TREATED WITH STREPTOMYCIN

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Ohio State M. J., 44: 816, (August) 1948

The first case, a Negro man, was treated with antimony compounds for 9 months for granuloma inguinale. At the end of this period Donovan bodies were still demonstrated in the open lesions. He was given 250 mg. of streptomycin every three hours until a total of 40 gms. was reached. The lesions were healed 29 days after therapy began.

Case 2, a Negro woman, had several large ulcers about the vulva showing Donovan bodies. She was given 28 gm. of streptomycin and discharged with the lesions healed.

Case 3 complained of menorrhagia of 4 months' duration and inguinal ulcers. A cervical biopsy revealed Donovan bodies. She received a total of 56 gms. of streptomycin. The cervical bleeding stopped as soon as therapy was begun and the ulcers began to heal.

Case 4 presented ulcerating lesions around the vulva and gluteal folds. By the time a total dose of 22 gms. had been reached the lesions were healed.

There was no recurrence in any of the 4 cases.

(The most popular treatment of granuloma inguinale has for a long time been the employment of antimony, commonly carried out by the intravenous injection of tartar emetic. If the splendid results reported in the 4 cases of Mason and Welsh through the use of streptomycin are confirmed by others, there would seem to be no doubt as to its superiority over antimony, the results of which have not always been striking.—Ed.)

COMPLETE CONGENITAL ABSENCE OF THE VAGINA ASSOCIATED WITH BILATERAL HERNIAE OF UTERUS, TUBES AND OVARIES

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Brit. J. Surg., 36: 99-100, (July) 1948

The patient, aged 20, was admitted to the hospital complaining that she had never menstruated. The breasts were well developed, pubic hair was normally distributed and the build was generally feminine. A small hernia in the left

freely phagocytosed at the site of infection. Moreover, bacillus crassus has been cultured from extragenital locations and recovered from the blood.

(The so-called Lipschütz ulcers are relatively rare, and I myself have seen only a small number of them. They are usually round or oval, and quite clean looking. As the author states, the bacillus crassus is accepted as the etiological factor, and it is interesting that the same organism was cultured from the oral lesion described in the 13 year old girl, since gynecologists have ordinarily, I believe, thought of the Lipschütz ulcer as occurring only in the vulvar and introital areas. There would seem to be no justification for including these simple ulcers under the designation of aphthosis, which always conveys the idea of a fungus etiology. The genuine cases of *ulcers vulvae acutum* described by Lipschütz are always, in my own experience and that of most others, readily curable by almost any simple cleansing and mildly antiseptic form of local treatment.—Ed.)

troitus, the region of the external urethral orifice, or the posterior commissure. Rarely, the perineal and the anal region may also be involved. Gangrenous and miliary forms of the ulcer are described. The ulcer generally heals spontaneously within 2 to 3 weeks and a duration of more than 8 weeks is quite rare. The author presents a typical case occurring in a 13 year old virginal girl who also presented a feeling of burning in the mouth, paresthesias in the hands, feet and face, and a positive Chvostek sign bilaterally. *Bacillus crassus* was cultured from the lesion. No spirochetes or gonococci could be recovered. The lesion healed under local application of marfanil-prontalbin (sulfonamide) powder. A temperature elevation to 39° was currently observed. Aphthous ulcers were also observed in the mouth.

Numerous other similar cases have been reported in which acute vulvar ulcers are accompanied by systemic manifestations. Ulcerations in the mouth are especially common. Erythema of the extremities and the face have also been observed. Positive Chvostek signs and paresthesias in the extremities have also been reported, as well as acute iritis.

Bacteriologically, the *bacillus crassus* is a plump gram positive rod with square ends which may be found both intra- and intercellularly. This organism is also often found as a harmless saprophyte in the vaginal secretions. It has also, however, been reported in oral ulcers. It may be a secondary invader of the ulcerations produced by other diseases. Several authors have suggested that there is a generalized distribution of *bacillus crassus* in this condition. The ulceration has occurred in entirely well and healthy persons as well as in those with anemia, asthenia and vasomotor and endocrine dysfunctions. However, the syndrome will be favored by reduction of the general resistance of the organism. Frequently the patients will have a history of tuberculosis.

Neumann has listed vulvar ulcers under the term aphthosis. Such ulcers are sharply defined, with edges which are not undermined. They are not deeply excavated and the actual loss of substance is slight. They have a tendency to recurrence and a tendency to be associated with oral and skin ulcers in other locations.

This syndrome has also been described with genital, oral and skin ulcerations complicated by iritis. *Bacillus crassus* has never been described in ulcerations of this type. The etiology of this group is obscure.

All types of local and systemic therapy for aphthosis have been employed, including Sitz baths, peroxide irrigations, silver nitrate, x-rays, autovaccination, ultra-violet ray, salvarsan, cauterization, sulfonamides and vitamin B complex, as well as estrogens. In general, vulvar ulcerations are resistant to therapy but have a tendency to heal spontaneously, as previously outlined.

The differential diagnosis includes chancroid, agranulocytosis, erythema multiforme, pemphigus and Vincent's angina.

In conclusion, the *ulcus vulvae acutum* may be differentiated from similar lesions (which may be lumped under the name of aphthosis) by the presence of *bacillus crassus* in the former. The author believes that *bacillus crassus* is the etiological agent because it can be cultured with such regularity and because it is

One cannot, at the present time, be justly accused of reactionarianism if one expresses uncertainty as to the future role of cytological diagnosis, or doubt that it will ever become more than a screening test. Even in the latter sense, it should be employed only by those with really adequate training, which is certainly not the case at present. And yet the wide propaganda for the method is creating a demand for it which can simply not be taken care of by the handful of trained cytologists now available. The ideal plan would be to explore fully the possibilities of the method only in those well organized clinics and cancer detection centers with adequately trained personnel, since its general adoption by practitioners is at present simply impracticable.

As a matter of fact, it is my feeling that the anti-cancer campaign has gotten a bit out of balance in the disproportionate emphasis being put on preclinical and preinvasive lesions. If Stage I cases, in which the diagnosis can almost always be easily made without smears by biopsy and the universally available pathological examination, and which are highly favorable for treatment, make up only 10 per cent of all cases, only a fraction of 1 per cent would represent the group which has been getting the bulk of the publicity. It is my considered opinion that if we could substantially increase the proportion of Stage I cases, the lives of many more women would be saved than would be possible by even far wider practice of vaginal cytology than exists at present. Are we losing sight of the woods for the trees? —Ed.)

EARLY DIAGNOSIS OF CANCER BY STUDY OF EXFOLIATED CELLS

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J. A. M. A., 138: 469-474, (Oct. 16) 1948

The writers' experience in the Vincent Memorial Laboratory in the years 1942 to 1947 is based on the examination of vaginal smears from 5,621 women, of whom 492 had uterine cancer. All figures are based on the initial smear report. The series includes 113 cases of endometrial carcinoma, in 83 of which diagnosis was made by smear, an error of 26.5 per cent; and 354 cases of cervical carcinoma, in 317 of which diagnosis was made by smear, an error of 10.5 per cent. There were 69 cases of positive smears not confirmed at pathologic examination, or a "false positive" error of 1.3 per cent.

In a group of 30 cases of preinvasive carcinoma of the cervix, the initial vaginal smear was positive in 23. Biopsies were performed for 27 patients. The initial biopsy was positive in 13, questionable in 4, negative in 8, and in 2 cases no tissue was obtained. Thus, in this series, the initial vaginal smear proved significantly more accurate than did the initial biopsy in detecting preinvasive cervical cancer.

Graham, Sturgis and McGraw, in comparing the accuracy of the vaginal smear and biopsy in 181 cases of proved epidermoid carcinoma of the cervix, found that the initial biopsy was correctly positive in 90 per cent; the initial vaginal smear was correct in 91 per cent. The 2 methods combined achieved a diagnostic accuracy of 99 per cent.

The results of screening in a total of 358 women, each examined by a single

THE UTERUS

CYTOLOGY: A DIAGNOSTIC METHOD IN EARLY CARCINOMA OF THE CERVIX

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South. M. J., 41: 706-711, (Aug.) 1948

The author summarizes the values of the routine employment of cytological studies in the detection of carcinoma of the cervix. Through this method, the diagnosis may primarily be made when the growth is in the incipient stage, and before the onset of symptoms or signs. The positive cytological test maintains the acute interest of the clinician in the patient, in spite of the negative biopsy report, until the diagnosis is clarified. The accuracy of the test is 98.5 per cent positive or negative when the cytologist is competent and conscientious and when repeated tests are made in suspicious cases, whether the suspicion is aroused by history, physical findings or the appearance of the cells, and when the "selective method" (Ayre) of obtaining the material is used. The test may be made easily accessible to patients in their own communities. It may also be used as a reliable check on the efficacy of irradiation therapy.

The making of a diagnosis on the basis of one cell has been viewed by some with alarm. However, the author emphasizes that the cytologist makes no such diagnosis, but reports finding a malignant cell and leaves it to the clinician to translate this report, either confirming it or rejecting it by biopsy, and the treatment of the patient is left to his judgment.

The writer briefly presents two cases. The first case illustrates that the diagnosis of cancer can be made by cytological study when the tumor is in its incipient and curable stage. The second case illustrates how the clinician's interest was maintained by a suspicious smear, in the face of a negative biopsy, which later proved to be due to a malignancy. 4 figures.

(The author is an enthusiastic advocate of vaginal cytology in the detection of cervical cancer, but I do not think that many would place the accuracy of the test, as he does, as high as 98.5 per cent positive or negative. However, he is conservative in emphasizing that the cytologist can only report the finding of malignant cells, leaving the decisive diagnosis for biopsy. Nor can the cytologist determine whether the malignant cells have their source in an early invasive lesion or from one which is still in a preinvasive and therefore not clinically malignant phase. Everyone agrees that cancer is an exfoliative lesion, that cancer cells can be found in the vaginal or cervical smears in a high proportion of cases, that the method is of great value as a screening test, but that it cannot replace biopsy as a decisive method of diagnosis. On the other hand, biopsy has definite limitations when the cervix exhibits no suspicious target lesion, since even with multiple excisions a preclinical lesion may still be overlooked. It is here that surface biopsy rather than cervical smear can play a valuable supplementary role, as I have repeatedly discussed on former occasions.

that the method is not diagnostic, that smear findings are not to be made the basis for treatment, and that positive findings merely point the way to more intensive and more diagnostic study, especially biopsy. The fewness of adequately trained cytologists and the time and money required for such studies have been obvious drawbacks to any general utilization of the method. This had led some to deplore the widespread publicity it has received even in the popular press, since it might create a widespread demand which under existing conditions simply cannot be taken care of. Nor are the definite limitations of the method usually made clear in these popular presentations, the woman reader commonly getting the impression that the question of whether or not she has cancer can easily be settled by simply taking a vaginal smear. The screening possibilities of the method should be fully explored by clinics fully equipped to do so, and it would seem almost better to utilize only such clinics as the workshops for this interesting clinical research problem. The method is still surrounded with too many limitations and pitfalls to be recommended for general adoption, even if the latter were possible, which is not the case at present. If the Toledo group furnishes another workshop of this kind, the movement deserves commendation and emulation.—Ed.)

DIAGNOSIS OF PRECLINICAL CANCER OF THE CERVIX: CERVICAL CONE KNIFE: ITS USE IN PATIENTS WITH A POSITIVE VAGINAL SMEAR

J. E. AYRE

Royal Victoria Hospital, McGill University, Montreal

J. A. M. A., 138: 11-13, (Sept. 4) 1948

The vaginal smear and "surface biopsy" methods of diagnosis offer valuable means of uterine cancer control by early detection. This presents the problem of confirmation by biopsy. Indiscriminate hysterectomy on the basis of positive smears without biopsies may cause this important advance in diagnosis of cancer to fall into disrepute.

The cervical cone knife is presented as a practical instrument to permit precision biopsies of the squamocolumnar junction in preclinical cervical cancer, introducing the "ring biopsy." Proper application of this instrument permits the excision of the entire squamous margin of the junctional region without necessitating a cervical amputation or a hysterectomy. Multiple or serial sectioning of this ring of tissue enables a precise and accurate diagnosis of squamous cancer in the cervix. The author presents instructions for the use of the cone knife.

To avoid needless radical surgery and treatment and yet to insure adequate protection of the patient against cancer and to preserve the valuable function of the cytologic study in cancer detection, the author lists recommended steps in diagnostic treatment in the presence of a positive cytologic test. 1 figure.

(Surface biopsies of the cervix are of great supplementary value in the diagnosis of pre-clinical stages of cervical cancer, especially in those cases in which vaginal smears have been

vaginal smear, yielded 6 positive smears, 5 of which were confirmed by pathologic examination—carcinoma *in situ* of the cervix in 4 and endometrial cancer in one case. Of the 4 patients with cervical cancer, no gynecologic symptoms were present in 2 and the cervix was normal to visualization in all.

The authors conclude that a positive smear demands that every possible effort be made to establish the diagnosis. Radical therapy is justified, however, only if confirmatory evidence is obtained. A negative smear should never outweigh other evidence in favor of malignant disease. While examination of fixed tissue remains the final criterion of malignant disease, evidence has been presented that in the cervix cancer may be detected earlier by cytologic examination than is possible by any other means.

(See comment on following abstract of paper by Hufford and Burns.—Ed.)

PAPANICOLAOU TEST IN THE EARLY DIAGNOSIS OF UTERINE CANCER

C. E. HUFFORD AND E. L. BURNS

Toledo, Ohio

Ohio State M. J., 44: 900-903, (September) 1948

The Academy of Medicine of Toledo and Lucas County has initiated a program using the vaginal smear in the early detection of uterine cancer. Several preparatory steps were necessary in setting up the program. First, it was necessary to educate the pathologist in evaluating the smears. This was done through group study meetings and the circulation of sets of slides. Secondly, technicians were sent to study under Papanicolaou and were trained in the staining technique, also in examining the smears in order that they could screen normal cases for the physician. While diagnosis of an abnormal slide cannot be left to the technician, this screening process is an aid in a large scale program. Thirdly, the practising doctors were informed of the method and its limitations. Finally, the women of the city were encouraged to co-operate by enrolling in the program. The response was so great that restraint had to be used in order to keep the new program from growing at too rapid a pace for the available personnel.

The Academy maintains a registry of all patients examined and stocks all doctors with triplicate smear request forms. The pathologist's report is returned to the requesting doctor and also recorded in the registry at the Academy which in turn notifies the physician when the patient is due for another 6 months pelvic examination and smear.

During the year of operation results have been encouraging and the authors feel that this type of program would be suitable for other communities.

(Everyone appears to be agreed as to the value of authoritative vaginal smear examinations as a screening test, and all of those who have had most experience with it emphasize

tion accomplishes a complete removal of the uterus and adnexa, the entire broad ligaments and paravaginal tissues, the pelvic lymph nodes, lymph channels and areolar tissues about the common iliac, external iliac and hypogastric vessels, the lymph nodes and areolar tissues in the obturator fossae, the areolar tissues on the posterior and inferior lateral surfaces of the bladder wall. And, finally, practically the entire visceral and parietal peritoneum with its subjacent areolar tissues is removed.

The author discusses procedures for excision of involved viscera adjacent to the cervix in instances of advanced carcinomas of the cervix. These procedures are capable of affording a degree of palliation not possible by other known measures in the face of previous failure of irradiation with or without conservative operation in these patients. (a) When the disease is still apparently confined to the cervix and upper vagina, radical panhysterectomy with pelvic lymph node resection can still be performed. (b) When there is local recurrence and rectal invasion, complete excision of the vagina and uterus and invaded portion of rectum is feasible with reconstitution of the rectum by end to end anastomosis. (c) When there is recurrence and bladder invasion, the uterus, vagina and entire bladder may be resected with bilateral ureteral implantations into the colon. (d) When bladder and rectum are both involved, the uterus, vagina, bladder and rectal colon may all be removed "en masse."

It is shown that, with modern supportive measures for the surgical patient, selection of patients for operation can be quite appreciably reduced in comparison to the selection exercised in the past. Since September, 1947, every patient at Memorial Hospital with carcinoma of the cervix is evaluated as a surgical problem. If there is clinical or roentgenologic evidence of spread beyond the pelvis (not including inguinal node involvement), the situation is regarded as inoperable. From September, 1947, to April, 1948, there have been 81 patients with carcinoma of the cervix, in 73 of which operation was performed, or an explorability rate of 90 per cent.

Furthermore, surgical mortality can be kept at such a level today that this can no longer be held as a major deterrent to the surgical approach in cancer of the cervix. The overall mortality in the series of 73 consecutive and unselected cases mentioned above was 5.5 per cent. The mortality is confined to the group presenting the most advanced local stages of the disease. In the group of 49 patients who had the radical operation, and in 12 instances of which there were additional resection of the viscera, the mortality was 2.0 per cent.

(The revival of radical panhysterectomy, with extensive gland incision in some clinics some years ago caused not a little lifting of eyelids among a good many gynecologists, in spite of the fact that it was advocated for only a selected group of favorable cases, chiefly those of Stage I. It has already been demonstrated that the primary mortality in these extensive operations can be kept very low by utilization of such modern advances as transfusions and antibiotics, although it is still too early to form any clear judgment as to how the ultimate results will compare with those of radiotherapy in the same clinical groups.

More startling is the concept of surgery in very advanced cases, those in which radiotherapy can offer slight hope indeed. As a matter of fact, radiotherapy has often been used in such cases with the feeling that it is purely palliative, and even for this purpose often of

definitely positive, and in which there is no evident local cervical lesion to furnish a target for direct biopsy with the scalpel or punch. In the presence of a suspicious lesion, it would be a serious omission not to subject it to direct biopsy, although even then surface biopsy may yield interesting and valuable information. The principle is a very old one, having been used by Schiller nearly a quarter of a century ago and no doubt by others before him. I myself have employed it as a routine in every vaginal operation for nearly 2 years. Various technics can be employed. That described by Ayre is essentially a small and superficial scalpel conization, and while I am sure it yields *satisfactory tissue*, and while I think it definitely superior to the cervical smear technic formerly advocated by him, it has the minor disadvantage of often causing moderate bleeding, so that it is often followed by conization of the Hyams type. The method of surface paring of the cervix and lower endocervix which I have several times discussed in these pages seems to me simpler and more satisfactory. Scheffey also uses a procedure quite like Ayre's, while others prefer a more extensive conization of the usual type and, when hot on the trail of something interesting, some use tracheloplasty or even trachelectomy. All these methods serve to illustrate the intensiveness of the search which must often be made when the cervix seems grossly normal or almost normal, but when the vaginal smear suggests that there is "something doing" somewhere in the cervix. Studies of this sort are ordinarily limited to the well organized and well equipped clinics, being scarcely feasible at present among practicing gynecologists in general. Cases in this early preclinical and sometimes preinvasive group constitute only a tiny fraction of all cases of cancer, and I believe it is still as true as ever that not many cases of clinically early type will be overlooked by simpler clinical methods, with the accent on the true and tried method of biopsy.—Ed.)

THE SURGICAL TREATMENT OF CANCER OF THE CERVIX UTERI (A RADICAL OPERATION FOR CANCER OF THE CERVIX)

A. BRUNSCHWIG

Cornell University Medical College and Memorial Hospital Center for Cancer and Allied Diseases, New York, N. Y.

Bull. New York Acad. Med., 24: 672-683, (Oct.) 1948

A review of the results achieved at the Memorial Hospital in the treatment of cancer of the cervix by irradiation from 1934 to 1941 reveals a more or less static situation in that about 28 per cent of all patients, year after year, were afforded a 5-year survival. Therefore, since the majority of patients developing cancer of the cervix continue to die of this disease, it follows that some consideration might be given to other forms of therapy. The only other form of therapy of proved efficacy is surgery. Present day surgery has not been systematically exploited in the treatment of cervical cancer. Since carcinoma of the cervix is a lesion that remains relatively localized for prolonged periods and does not present distant metastases in the large majority of instances at the time the clinician first encounters the disease, the lesion would appear favorable for surgical attack.

A radical operation is described for excision of carcinoma of the cervix which has not involved the bladder or rectum. This procedure would appear to be more extensive than hitherto carried out for this type of neoplasm. The opera-

an almost constant level of overall cure rates for the period of 8 years with no tendency to rise in spite of the increasing frequency of patients in the early stages of the disease.

Four more tabulations according to the stage of the disease are included. For the 200 Stage 1 cases the relative cure rate was 53.0 per cent. There is no consistent improvement in results shown in Stage 2 and the cure rate for the 339 patients is 33.1 per cent. The 8 year average rate for Stage 3 for 454 patients was 17.4 per cent.

The authors point out that some classifications had to be made from the patients' charts as the League classifications were not used earlier. This fact along with the small number of patients in each stage makes significant statistical analysis impossible.

However, the authors feel that there appears to be little improvement in the irradiation therapy results in the management of carcinoma of the cervix.

(While the results reported in this large series compare favorably with those reported from other clinics, it is rather discouraging that the cure rates in Stages 2, 3 and 4 have shown no worthwhile improvement for many years, since these represent the great bulk of those which come under observation, and since in this very large group no other plan of treatment than irradiation can usually be offered, according to the concept of almost all clinics. On the other side of the picture, the classification of 200 out of 1072 cases as Stage 1 gives a higher incidence of this relatively favorable stage than is noted in most reports, and justifies the feeling of many gynecologists that on the whole more comparatively early cases are now coming under observation, probably as the result of popular education. The tempo of the educational campaign has been tremendously stepped up in the past few years, chiefly under the leadership of the American Cancer Society. It is to be hoped that this incidence will be reflected in the stage classification figures of the next few years. Here lies the most hopeful avenue for a lessening of cancer mortality.—Ed.)

SARCOMATOUS DEGENERATION OF A MYOMA FOUND AT CESAREAN SECTION: REPORT OF A CASE

M. LOUISE BENEFIELD

Long Beach, California

Ann. West. M. & S., 2: 377, (August) 1948

The patient, a 28-year-old woman, was first seen for a premarital examination. A diagnosis of a fibroid tumor of the uterus was made and she was advised not to wait too long if she wanted children.

Two months later she returned with symptoms of early pregnancy. Pregnancy was uneventful. Labor began normally but after 12 hours the fetal heart rate was irregular and the presenting vertex was not engaged. At a sterile vaginal examination a diagnosis of occult prolapse of the cord was made. Shortly afterwards a male infant was delivered by low cesarean section. After closing

questionable value. In the early days of radium, the surgeon was likely to skim off the cream by operating on a chosen highly favorable group, turning over the great bulk of others to the radiologist. And now Brunschwig reports that every patient at Memorial Hospital is evaluated as a surgical problem, and that 73 of the 81 patients admitted in a given period were treated surgically. One can scarcely imagine a more revolutionary concept, since many of these cases are of the type commonly accepted as hopeless and since even in these cases the operation is devised for a curative rather than a palliative goal.

This concept requires great courage on the part of the surgeon, much more so than that in operating upon a small group of favorable type. The operation which Brunschwig has already done in a considerable group of hopeless cases and which some have jestingly spoken of as the All-American operation, consists essentially of a complete pelvic excochleation, with removal of the whole genital tract as well as the bladder and rectum, and with colostomy and the transplantation of the ureters into the bowels. No one would expect many, if any, cures in cases of this group, and it is as yet too early to be sure that the few cases who have survived for an appreciable time are cured. The chief burden on those who do this operation will be to demonstrate that the terminal days of these almost hopeless cases are sufficiently ameliorated to justify resort to a procedure of this magnitude. I doubt whether many will adopt this procedure in the immediate future and certainly the operation should never be undertaken except in the most highly organized and well equipped operating rooms, with ample provision for the huge amounts of blood for the numerous transfusions always required.—Ed.)

FIVE YEAR END-RESULTS OF IRRADIATION THERAPY OF CANCER OF THE CERVIX UTERI AT THE MEMORIAL HOSPITAL

E. W. MUNNELL AND A. BRUNSCHWIG

Memorial Hospital, New York, N. Y.

Surg., Gynec. and Obst., **87**: 343-348 (September) 1948

A report is made of 1,072 cases of primary carcinoma of the cervix in patients treated from 1934 to 1941. The report was submitted to the League of Nations Health Organization and made in accordance with their classification and regulations, i. e., only carcinoma of the cervix treated with radiological therapy is included. A 5-year survival is classified as a cure.

Treatment with X-ray varied. The "massive dose," "divided dose," and "pyramidal dose" techniques were used. The "divided dose" was felt to be superior. Roentgen therapy was a supplement to the cervical tandem or a vaginal bomb form of radium therapy.

Of the 1072 patients examined, 96.7 per cent were treated. Table 1 gives reasons for non-treatment. Table 2 shows the total treated patients broken down into the 4 stages. It is interesting to note that later in the study there are more patients in the early stages.

The overall end results for a 5-year survival without breakdown into stages of extent of cancer is presented in the fourth table. The relative cure rate based on cures per total patients in all 4 stages treated was 28.6 per cent. There is

an almost constant level of overall cure rates for the period of 8 years with no tendency to rise in spite of the increasing frequency of patients in the early stages of the disease.

Four more tabulations according to the stage of the disease are included. For the 200 Stage 1 cases the relative cure rate was 53.0 per cent. There is no consistent improvement in results shown in Stage 2 and the cure rate for the 339 patients is 33.1 per cent. The 8 year average rate for Stage 3 for 454 patients was 17.4 per cent.

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the uterus, a pedunculated fibroid measuring 7 by 5 by 5 cm. was dissected from the corpus. The postoperative course was smooth and easy and the patient was discharged on the eighth day.

The pathologist's report of the specimen indicated that there was variation in the size and shape of the cells and that mitotic figures were present. There was vascular degeneration and some necrotic tissue. The diagnosis was a low grade leiomyosarcoma.

(The diagnosis of sarcomatous change in a myoma is often obvious enough, but there are cases in which pathologists will differ as between benign cellular myoma and sarcoma of a very low histological degree of malignancy. The difficulties are apt to be greatest in the submucous types of myoma, chiefly because many of these show varying degrees of inflammatory infiltration and degeneration. In the author's case the pedunculated tumor was presumably subserous and not submucous, and the note that "there was variation in the size and shape of the cells and that mitotic figures were present" appears to justify the diagnosis of low grade leiomyosarcoma. In rare cases mitoses have been found in benign myomas (Hartz) and the size and shape of the cells in myomas must be interpreted on the basis of the angle of section of the constituent bundles. It is probable, however, that other nuclear changes than mitoses, such as hyperchromatosis, were also noted in this case. It would be an interesting case to follow up. If only the one myoma is involved, and this was completely removed, it would seem highly probable that recurrence might not occur with a tumor of this apparently low degree of histological malignancy.—Ed.)

INOPERABLE SARCOMA OF THE UTERUS: TEN YEAR SURVIVAL OF A PATIENT

S. P. PERRY, W. D. HADEN, JR. AND A. L. HUNTER

Guthrie Clin. Bull., 18: 11-13, (July) 1948

It is pointed out that irradiation treatment of inoperable malignancies of the abdomen is often given in inadequate amounts, when actually, palliative treatment should be given with a cure in mind.

The patient whose case is presented in this paper was 9 years old when first seen with complaints of lower abdominal pain, a mass in the lower abdomen and painful urination. Operation showed the mass to be uterine, extending one inch past the umbilicus. Many small loops of gut and colon were adherent to the mass. Separation caused gross hemorrhage and the tumor was considered non-resectable. Biopsy was taken and the abdomen closed. Sections of the removed tissue presented the appearance of a round cell sarcoma.

The patient was started on roentgen therapy 3 weeks postoperatively, with a daily dose of 300 r. Treatment was given through two anterior pelvic portals and one posterior portal. A total dose of 6000 r was given. The patient had a very marked irradiation reaction, but by keeping her hydrated it was possible to complete treatment. There was marked decrease in the size of the abdominal mass and at the time of discharge, the mass was no longer palpable. The pa-

tient has been followed regularly, and when seen in 1945 at the age of 16, there was no evidence of malignancy. She had menstruated occasionally, very scantily and irregularly.

(This case illustrates the difficulty of predicting as to the course of malignant tumors, and the caution and flexibility which should form a part of prognosis. With many types the characteristically relentless progress leaves little doubt as to the ultimate result, but vagaries are often encountered, entirely aside from methods of treatment, and whether these are to be looked upon as adequate or inadequate. The authors are therefore wise in urging that, even though only palliation is hoped for, irradiation be given in amounts which would not, theoretically at least, exclude the possibility of cure.

An interesting feature of this case was that even after the extensive irradiation used in this prepuberal patient, the ovarian function was not permanently abolished, as she was having occasional menstruation 7 years later. It would seem likely that the function would later increasingly approach normality, as irradiation effects upon the ovary tend toward increasing attenuation with the passage of time.—Ed.)

GYNATRESIA: REPORT OF THREE UNCOMMON CLINICAL TYPES

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Cardiff Royal Infirmary and Welsh National School of Medicine, England

Brit. M. J., 2: 555-558, (September) 1948

The first patient aged 31, complained of right sided abdominal pain occurring at irregular intervals for 12 months. She had never menstruated. The cervical canal seemed to be a blind depression. At laparotomy the uterus was found to be about the size of a 3 months' pregnancy and about 4 oz. of old menstrual blood were released from it. The cervix was opened and a canal fashioned over an indwelling catheter. Two years later the patient was menstruating normally. Congenital occlusion of the cervix is a rarity and is usually associated with a non-functioning uterus.

The second patient, aged 13, suffered from severe dysmenorrhea. The pain was localized to the left iliac fossa and the left leg. An abdominal mass filling the left pelvic cavity was palpated. At operation the tumor was discovered to be the distended left horn of a bicornate uterus. Blood had been forced into the tube to form a hematosalpinx. About $\frac{1}{2}$ pint of blood was released and the left horn was excised. Such a uterus bicornis seldom undergoes menstrual changes. Where a hematometra occurs intense pain soon after puberty is of diagnostic value.

The third case is one of hydrocolpos in a 14-year-old. The vagina was occluded by a retrohymenal membrane. When this was excised $1\frac{1}{2}$ pints of turbid watery fluid escaped. Hydrocolpos is most common in newborns and just before puberty; at both times the uterine glands are secreting and are controlled by estrogen. The author urges that all female babies be inspected for vaginal occlusion at birth in order to avoid this condition. 1 figure.

(Of these 3 interesting cases of gynatresia, I was especially interested in the second, chiefly because I had recently encountered an instance of this general type, occurring in a girl of 16 who suffered with intense and prolonged dysmenorrhea. It was thought to be of primary type, since rectal palpation before anesthesia revealed no gross abnormalities. Since there had been no improvement following simpler methods of treatment, a presacral sympathectomy was decided upon. Before the abdomen was opened, a pelvic examination was done under anesthesia, revealing a small but definite mass at the left of the fundus. This was found to be a rudimentary uterine horn which was filled with blood, so that it at first suggested an endometrial cyst or a tubal gestation. The retention of blood was due to the fact that there was apparently an atresia between the small cavity of the rudimentary horn and the uterus proper, the accumulated menstrual blood in the horn evidently exciting the intense dysmenorrhea. While cases of this type are of course rare, their possibility must be borne in mind in the interpretation of cases of unusually severe dysmenorrhea in very young girls. Examination under anesthesia may yield worthwhile information in this respect.—Ed.)

HISTOCHEMICAL STUDIES ON ABNORMAL GROWTH OF HUMAN ENDOMETRIUM

I. ALKALINE PHOSPHATASE IN HYPERPLASIA AND ADENOCARCINOMA

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for Women, New York, N. Y.*

Cancer, 1: 248-251, (July) 1948

Alkaline phosphatase activity has been studied histochemically in a series of hyperplastic and carcinomatous human endometria. The enzyme has been found in all cases of hyperplasia, the amount and distribution varying without relation to either the degree of hyperplasia or the menopausal status of the patient. On the other hand, in adenocarcinoma, a definite inverse relationship exists between the degree of tumor activity, as judged by the usual histopathological criteria, and the over-all phosphatase activity. In undifferentiated carcinomas the tumor cells contain little or no enzyme. As in hyperplasia, differentiated tumors exhibit variable phosphatase activity that is unrelated to either the morphological patterns within the individual tumor or the menopausal status of the patient. 4 figures.

THE ADNEXA

LARGE OVARIAN CYST

J. W. NIXON AND W. A. WICHERN, JR.

San Antonio, Texas

South. M. J., 41: 774-776, (Sept.) 1948

The authors present a case of a huge ovarian cyst which, with its contents, weighed 108.4 pounds.

The patient was a 33-year-old Mexican woman who had noticed progressive enlargement of her abdomen for 7 years, with a more rapid increase in size in the 5 months prior to admission. Because of the size of her abdomen, she experienced extreme weakness and dyspnea and was unable to walk. There was edema of the legs. The menstrual history had been normal until the onset of swelling, at which time she also developed amenorrhea. Physical examination showed the patient to be very debilitated. All the thoracic viscera were displaced upwardly. The pulse was 120 and the blood pressure 120/90. The abdomen was tense and there were many dilated superficial veins. There was a fluid wave present.

A paracentesis was performed and 45,500 cc. of dark brown fluid was removed over a 48-hour period in an interrupted manner. Over the next several days the patient seemed improved. She then began complaining of chest pain, weakness, nausea and vomiting, and went into shock. This was treated with temporary success, but she returned to a state of shock despite treatment, and died on the seventh hospital day.

At autopsy, a large pseudomucinous papillary cystadenoma was found arising from the left ovary. The lungs showed congestion and occasional small thromboses. There was myocardial fragmentation, and degeneration and hemorrhage in the liver, kidneys and adrenals.

On the basis of this case, and from information gathered from the literature, the authors feel that the course of treatment for large ovarian tumors should first consist of gradual decompression via paracentesis, improvement of the patient's general condition, and then operative removal of the tumor. 2 figures.

(While a cyst weighing 108.4 pounds is certainly not to be sneered at, many much larger ones have been reported. The largest on record, so far as I know, was that reported by Spohn of Texas, the state of tall men and tall stories. (Cited by Lynch, *Pelvic Neoplasms*, D. Appleton & Co., N. Y., 1922.) However, it would appear that the author cheated just a little in estimating the size, since before the tumor was removed it had been tapped a few times, and the weight of the removed fluid was added to the weight of the tumor at operation, by which time additional fluid had no doubt been accumulated. Even so, it seems probable that this tumor may well have been the largest recorded. Lynch, in his monograph on *Pelvic Neoplasms* (D. Appleton & Co., N. Y., 1st ed., 1921) collected quite a group of these monster ovarian cysts, including quite a number over 200 pounds. In

some of these, the same butcher's thumb method of weight computation mentioned above was used. Those were the good old days, as it is only rarely that women in this surgically educated era allow tumors to grow to such enormous size. Even now, patients often eagerly ask the surgeon how much their tumors weighed at removal. The surgeon who errs on the conservative side is probably not fond of fishing.—Ed.)

FERTILITY AND DYSGERMINOMA OVARII

T. L. BALL AND C. T. JAVERT

Cornell University Medical College and The New York Hospital

J. Clin. Endocrinol., 8: 294-298, (August) 1948

Pregnancies have occurred in the presence of or after the removal of dysgerminomata. These rare ovarian tumors are usually on the right side and do not necessarily cause sterility. They are presumably neutral and neither masculinize nor exaggerate feminine characteristics. It would appear that the tumors cause sterility in normal females only in so far as they destroy ovarian tissue or cause tubal occlusion by pressure.

The case of a 39-year-old primigravida is reported. Twelve years prior to the pregnancy a tumor of the right ovary had been cured by right salpingo-oophorocystectomy. Post-operatively the patient received 4 X-ray treatments. The left ovary remained intact and menstruation occurred regularly.

The patient had conceived one year after marriage. She was delivered successfully by a mid-forceps operation in the 38th week of pregnancy following premature rupture of the membranes.

The possibility of subsequent pregnancies should be considered in the treatment of dysgerminoma. If the tumor is unilateral, the capsule intact and the opposite ovary and tube normal, a unilateral oophorectomy is indicated. Bilateral tumors necessitate radical surgery followed by radiation. The anaplastic characteristics of carcinoma are of little aid in arriving at a decision as to whether the tumor is benign or malignant.

(As the authors state, the report of quite a few cases of dysgerminoma in association with pregnancy indicates that tumors of this sort do not impose infertility upon the patient unless there are such adventitious factors as the authors mention. Moreover, there would seem to be no reason why pregnancy might not occur after the successful removal of a dysgerminoma, as in the authors' case. I agree with the justifiability of conservative unilateral operation in cases in which the tumor is of small or of moderate size and possesses an intact capsule. To say that there is no hazard whatever of recurrence or metastasis in such cases would not be justified, but the risk is sufficiently small to warrant conservative operation in the young patients in whom most such tumors occur.

See also comment on following abstract.—Ed.)

OVARIAN DYSGERMINOMA WITH A REPORT OF TWO CASES

J. A. SPENCER AND P. J. REEL

Stanford University Medical School, San Francisco, California

Ohio State M. J., 44: 817-818, (August) 1948

In the first case, a 13-year-old girl was admitted complaining of vaginal bleeding of 6 weeks' duration. Her periods began at 12 years and had previously been normal. Other symptoms were loss of weight, dizziness, and pain in both legs. Examination revealed a fixed tumor mass filling the pelvis and extending to the umbilicus. An exploratory laparotomy was performed but only a small portion of the tumor could be exposed because of intestinal adhesions. A block biopsy was removed and the pathologist's report showed a highly malignant dysgerminoma. The patient received 2,000 roentgen units and the tumor mass was reduced, but the patient died 6 weeks after discharge.

The second patient, a 14-year-old girl, complained of progressive enlargement of the abdomen, loss of weight, lower right quadrant pain and frontal headaches. A pelvic tumor mass was palpated and extended 6 cm. above the umbilicus. At laparotomy it was seen that the tumor rose from the left ovary and was densely bound to the posterior and postero-lateral pelvic walls. Bilateral salpingo-oophorectomy and supra-vaginal hysterectomy were done after a frozen section diagnosis of dysgerminoma of a malignant type.

The patient received 2,400 roentgen units and was discharged with improvement. After 5 years she is well and shows no evidence of disease.

(That dysgerminoma of the ovary is more malignant than some pathologists seem to believe is indicated by the first of the 2 cases reported in the above paper. In this case the tumor was a very large one and had probably penetrated its capsule, so that the fatal result is not surprising. However, recurrences have not infrequently occurred even with much smaller tumors with intact capsules. Tumors of this group appear to be fairly radiosensitive. The first case ever recognized in our Department occurred in a 7 year old colored child, the tumor filling most of the abdomen and infiltrating surrounding organs. Complete removal was impossible, and the residual tumor mass responded to radiotherapy but did not completely disappear. Later it again grew rapidly, with again shrinkage after radiotherapy, although a residual mass was always palpable through the rectum. After several courses of radiotherapy, the patient succumbed at the age of 10. See also comment on preceding abstract.—Ed.)

FEMALE UROLOGY

UTEROVESICAL FISTULA FOLLOWING THERAPEUTIC ABORTION: A NEW OPERATION

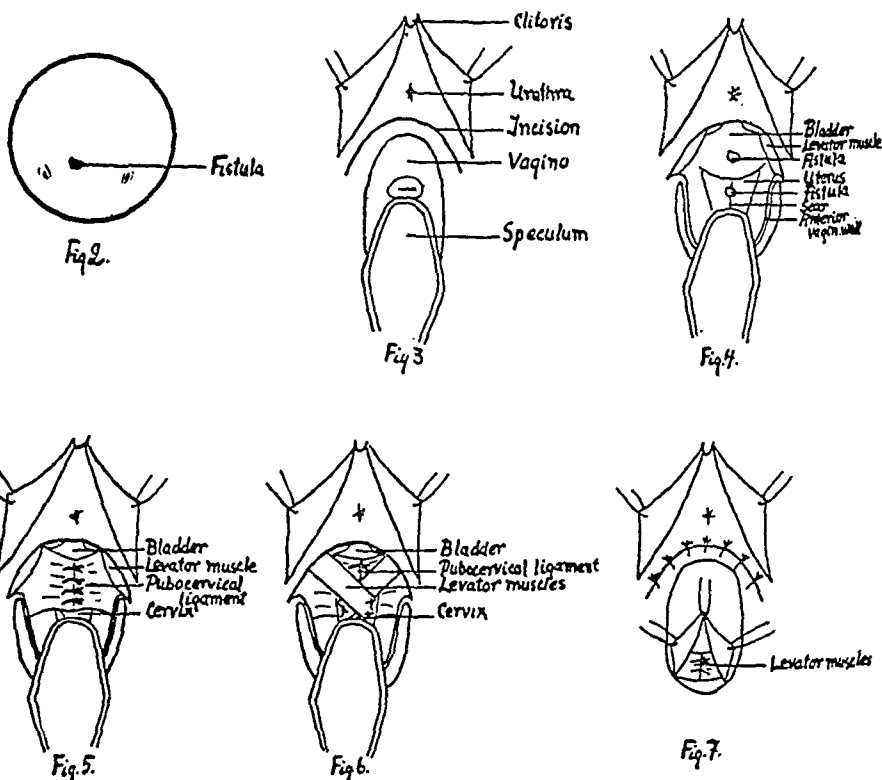
A. INGELMAN-SUNDBERG

Women's Clinic, Karolinska Sjukhuset, Stockholm, Sweden

Gynaecologia, 126: 274-280, (Nov.) 1948

The author reports a case of uterovesical fistula. The lesion was the result of a therapeutic abortion performed with version and extraction of a female fetus, 24 centimeters in length, after anterior vaginal hysterotomy. The fistula was operated upon according to the author's new extravaginal method.

The urethra and the base of the bladder are exposed through an incision just under the urethra (Figs. 3-4). After suturing of the fistula, interposition is carried out by using the paravesical fascia and the levators (pubococcygeus muscles) which are divided (Figs. 5-6). In this way, two anterior portions are pro-



duced, being attached to the symphysis, and two posterior ones, attached in the region of the coccyx. The anterior portions are crossed and sewn fast to the cervix with silk or wire of stainless steel (Fig. 6). The posterior levator portions are located with a clamp through a longitudinal incision in the posterior vaginal wall. They are united in the midline in front of the rectum by means of a few heavy catgut sutures (Fig. 7). The mucosa is then sutured with fine catgut, and the vagina is well sponged with gauze powdered with microcrystals of sulfathiazole or penicillin. An indwelling catheter is left in place for about a week, the tampons being removed after 24-48 hours. 7 figures.

(This rare type of fistula has been most often treated by separation and mobilization of the bladder, followed by excision of the fistulous tract and separate suture of both the uterine and bladder orifices, although the technical difficulties involved might conceivably be considerable. In a small number of reported cases, such fistulas have closed spontaneously. The chief symptomatic characteristic of fistulas of this variety, aside from the leakage of urine, is the hematuria which occurs during menstruation. In the case described by Ingelman-Sundberg, the extensive, almost cartilaginous fibrosis and the difficulties of orientation apparently made it necessary to resort to the special technic depicted in the accompanying illustrations, and with apparently an excellent result.—Ed.)

OPERATIVE GYNECOLOGY

COMPLETE EXCISION OF PELVIC VISCERA FOR ADVANCED CARCINOMA: A ONE-STAGE ABDOMINOPERINEAL OPERATION WITH END COLOSTOMY AND BILATERAL URETERAL IMPLANTATION INTO THE COLON ABOVE THE COLOSTOMY

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Cancer, 1: 177-183, (July) 1948

The writer presents a radical operation devised for total excision of all pelvic viscera en masse for advanced carcinoma. As of April 10, 1948, 22 such operations have been performed. No selection was exercised, except that the disease be confined to the pelvis. The patients presented advanced cancer, and suffered from varying degrees of pain and other discomforts attributable to large masses of malignant tissue that had become infected, given rise to fistulas, and had previously received various forms of radiation therapy that had failed to control the growths. It is to be noted that all of these patients had been declared in the terminal stages of the disease.

Preoperatively, blood transfusions are given as necessary, and vitamins C and K are administered. Caster oil is given in the evening on the third and second days and magnesium sulfate on the following morning. Streptomycin is given orally for 2 days prior to operation. The day before operation, 8 gm. of sulfadiazine is given. At the beginning of the operation saline and then blood are administered intravenously.

In the abdominal phase of the operation, all pelvic viscera are excised, ligated and mobilized except for the attachments to the pelvic floor. The ureters are ligated well above any gross evidence of malignant involvement and are then implanted into the sigmoid colon; the mesopelvic colon is divided with preservation of the blood supply to the sigmoid. The abdominal wound is closed with the end of the sigmoid brought out through the incision.

The second, or perineal, stage consists of closing the vaginal introitus and anus, and of incising an area of perineum to include the anus and introitus, extending from the tip of the coccyx to below the clitoris. The dissection is carried upward, and the pelvic organs, en masse, are removed from the pelvis from below. The perineal wound is closed.

Postoperatively, continuous gastric aspiration is carried out for 72 to 96 hours. Penicillin and streptomycin are given for 3 to 5 days. Fluid balance is maintained by venoclyses.

Of the 22 patients submitted to this operation, 5 are considered to represent the surgical mortality, or 23 per cent. In view of the situations present in these unselected cases, the mortality in this original series is not considered excessive.

Management of the colostomy has been facilitated by the use of the Rutzen bag with its "cement" attachment to the skin. Urinary and alimentary excretion is accomplished normally through the colostomy.

Because of the advanced stage of their disease, it is not anticipated that many, if any, of these patients will survive for very prolonged periods. Two of the surviving patients did experience relief and returned to almost normal existence before they succumbed from metastases. Thirteen patients are living at this writing, and not one has regretted the operation.

From the author's experience, it is apparent that complete deperitonealization of the pelvis may be carried out and the small intestines permitted to descend into it without subsequent development of intestinal obstruction. 5 figures.

(Only a few years ago the all but universal therapy in carcinoma of all stages was irradiation, with only a few strongholds of radical surgery still left, and these practicing a considerable degree of selectiveness in picking cases for operation. The recent resurgence of radical surgery is still looked upon as a "noble experiment," and the majority of gynecologists appear to be willing to watch this experiment from the sidelines until more conclusive evidence of its advantages is available than is yet the case. But the operators of today are more selective now than those of preradium days, when the only alternative to operation was death by the palliative route. Only cases of Stage I and perhaps some of Stage II are selected for operation.

Until very recently anyone who would have suggested radical procedures in far advanced cases would have been both ridiculed and condemned. And yet Brunschwig emphasizes the fact that all of his patients had been declared in the terminal stages of the disease, and he also states that "it is not anticipated that many, if any, of these patients will survive for very prolonged periods." He himself therefore evidently looks upon the operation as a palliative one, though it will impress many as a very radical type of palliation. I recently heard some one unkindly describe the procedure as the radical removal of all the pelvic contents except some cancer cells. Each surgeon will have to decide for himself whether this radical palliative procedure is a justifiable one, even though death is the other alternative. Perhaps the consent of the patient should not be too much stressed, as patients with the intractable pain of advanced cancer would often as eagerly consent to permanent relief of their suffering through any form of euthanasia.

It is probably not necessary to warn against widespread adoption of this plan, since the operation is a huge one, requiring great skill and complete equipment including almost any amount of blood for the massive transfusions often necessary. All these requirements are met by Brunschwig and it will be interesting to see whether or not this particular experiment, far nobler and braver than that of radical operation in clinically early cases, will justify itself.—Ed.)

SIMPLE OPERATIVE PROCEDURES IN INTRALIGAMENTARY
TUMORS WITH NOTES ON PERITONEALIZATION OF THE
PELVIS FOLLOWING HYSTERECTOMY

K. BURGER

From The University Woman's Clinic of Würzburg, Germany

Geburtsh. u. Frauenhk. 8: 569-575, August, 1948

Burger traces the development of gynecological-surgical technic. He points out that any operative procedure will be simplified by proper preparation, a good knowledge of anatomy, and the use of as little suture material as possible.

Intraligamentary tumors are not so hard to manage as the literature would indicate. In operations upon intraligamentary tumors injuries to the bladder, ureters and rectum are to be avoided.

Burger's technic in the handling of intraligamentary tumors is as follows: After clamping off the tube, the round ligament and the uteroovarian ligament, these structures are cut away. The leaves of the broad ligament and the vesico-uterine fold are opened, thereby exposing the upper and anterior aspect of the intraligamentary tumor. The right hand of the operator is now passed below the lower posterior pole of the tumor and the latter is easily dislodged by upward pressure. Cervical myomata may be treated by grasping the corpus uteri and raising it as high out of the pelvis as possible. The tube, the round ligament and the uteroovarian ligament are then cut. The broad ligament and vesicouterine fold are then opened and often the cervical tumor will rise high out of the pelvis along with the corpus uteri. If it does not so rise it may be pushed out of the pelvis in exactly the same manner as an intraligamentary tumor.

Burger peritonealizes the cervical stump or vaginal cuff with a single suture. The round ligaments and adnexal stumps are attached to the cervix or vaginal cuff. This procedure uses the least possible suture material. Occasionally it may be necessary to attach the round ligaments to the cervical stump or vaginal cuff and then use a second suture for peritonealization.

Intraligamentary ovarian tumors may be attacked in the same manner as intraligamentary myomata. If the contents of the ovarian cyst should be spilled the delivery of the cyst may be facilitated by grasping the cyst wall with toothed forceps. If the intraligamentary cyst cannot be delivered in the manner already described for myomata, and if bursting of the wall of the tumor should occur, then Burger feels that the cyst should be emptied. The cyst lining at the bottom of the intraligamentary space will then become visible and may be grasped with forceps. Sometimes it will come away easily; more often it must be removed piecemeal. In any event, the entire cyst wall is removed and there is no possibility of a recurrence.

(While the procedures recommended by Burger are those which every experienced gynecologist would follow in the removal of intraligamentary tumors, their importance is worthy

of stress. To try to remove an intraligamentary myoma lying low in the pelvis by clamping the vessels external to the tumor would be likely to be disastrous, especially as the ureter could scarcely escape injury. If the broad ligament on the other side is free, such operations are often simplified and made far safer by going down on the free side, removing the uterus, and then drawing the tumor mass out of its deep bed between the layers of the broad ligament. Even this should not be done roughly, because such tumors often impinge on the ureter so closely that the latter can be brought up with the tumor mass.

As Burger says, similar "intracapsular" plans are often of great service in the removal of ovarian cysts which have become intraligamentary or retroperitoneal. On the left side such tumors may grow into the mesosigmoid, so that the bowel may stretch like a flattened ribbon over the tumor surface. In a recent case of my own, it was simply impossible to remove the large retroperitoneal tumor without injuring the blood supply of the sigmoid so irretrievably that resection of a loop of the bowel was necessary. Such cases, rare though they may be, simply emphasize that the training of the gynecologist must include preparation for the handling of pretty much all types of abdominal surgery. I am not at all certain that adequate correlated training of this sort is provided for in many otherwise excellent residencies in obstetrics and gynecology.—Ed.)

FURTHER EXPERIENCES WITH THE USE OF AMNION IN THE CONSTRUCTION OF AN ARTIFICIAL VAGINA

KARL BURGER

From the University Woman's Clinic of Würzburg, Germany

Zentralbl. f. Gynäk. 12: 1153-1158, 1947

The author reports 12 cases of absence of the vagina in which an artificial vagina was constructed. In 10 of these the artificial vagina was lined with amnion. This amniotic membrane is obtained at cesarean section. It is placed upon a sponge rubber prosthesis. No sutures are used to hold the amniotic epithelium on the prosthesis since the author feels that this disturbs the fixation of the epithelium to the vagina. On the 6th to 8th postoperative day the sponge is removed and an India rubber prosthesis is put into place. The latter is maintained for about a month, being removed for several hours daily. The family physician should digitally dilate the newly formed canal periodically.

If the dilatation is not carried out and the form not used, shrinkage of the newly formed vagina will occur. On the other hand, too vigorous dilatation is to be avoided lest a fistula into the rectum be established.

The danger of constriction of the artificial vagina at the level of the pelvic floor musculature is also present. This might theoretically be avoided by making a lateral, horizontal incision at this level. The author, however, has not employed such a method in any of his cases.

In the 10 cases in which the newly formed vagina was lined with amniotic epithelium a perfectly normal vaginal mucosa was established in which glucogen could be demonstrated and in secretions from which Doederlein's bacillus was present. Cases treated in this manner, when examined as early as the 5th to

8th postoperative day, show the newly formed vagina to be lined with a smooth slippery membrane which does not bleed upon light friction. Such cases were up and about by the end of the second week and frequently could be discharged at this time. On the other hand, the 2 cases in which the vagina was not lined required a much longer time for convalescence. In 1 case epithelization required 3 months. In the other, the upper end of the newly formed vagina was still granulating 176 days after operation.

Burger states that in his opinion the amniotic epithelium which is implanted in the artificial vagina takes hold there and eventually forms the new vaginal mucous membrane. He states, however, that others feel that it simply forms a temporary covering and facilitates the ingrowth of the vulvar epithelium. The exact method, however, is immaterial because the results achieved with amniotic membrane are so favorable that they justify the continuance of the method.

Other methods of forming an artificial vagina are discussed. Burger says that the best method is to use intestine, either small or large. However, this method is attended by a significant mortality and an appreciable incidence of postoperative infection. Another good method is to use skin to line the vagina. This in turn, however, leaves a scar upon the body; whereas it is equally simple to use amniotic membrane, leaving no external marks.

(The author of this paper visited this country as the honor guest of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons some years before the war. At that time he was the Director of one of the two Frauenkliniken in Budapest, where I had the pleasure of visiting him a year or so later. He was just beginning the method he describes in his paper of utilizing fresh amniotic membrane in the construction of artificial vaginas, although no case was available for demonstration during my stay. Dr. Burger, however, insisted on my taking with me one of the sponge rubber prostheses which he uses. It looks like the tip of one of the tall marsh plants known as cat-tails, even to the color. With the attached wooden handle, it is almost a foot in length, and the sponge rubber-covered portion, some 7 inches long, is approximately $1\frac{1}{2}$ inches in diameter. The purpose of the sponge rubber is that the amniotic membrane adheres to it without the use of sutures. A disadvantage that will suggest itself is that the operations must be planned when there is a cesarean section on tap. A theoretical advantage is that the amnion, like skin or vaginal mucosa, is of ectodermal origin, and, if it does actually take root, might be expected to result in more rapid epithelization than when no grafts at all are used. However, the results of the comparatively simple reconstructive operations of the Wharton type, even when no skin grafting at all is used, have been so good that it is perhaps not surprising that the Burger technic has not been resorted to in our own clinics. The same good results, in the minds of at least a good many American gynecologists, are observed with operations of the McIndoe type, in which pinch grafts are used, although such procedures will usually call for the cooperation of a competent plastic surgeon. I gather that Burger himself is not convinced that the amniotic epithelium actually takes hold, and that possibly it forms only a smooth temporary covering which promotes epithelization from the vulvar epithelium. The latter seems more probable, since even without any grafts the epithelization is usually pretty complete by 3 months. Furthermore, the new vaginal epithelium soon develops the same biological characteristics as those of normal vaginal mucosa, such as responsiveness to the ovarian hormones.—Ed.)

TOTAL VS. SUBTOTAL HYSTERECTOMY WITH SPECIAL
REFERENCE TO CARCINOMA OF THE CERVIX—
ANALYSIS OF 257 PERSONAL CASES

J. J. McDONOUGH

Youngstown, Ohio

Ohio State M. J., 44: 914-917, (September) 1948

The desirability of total hysterectomy is presented. In the 257 cases discussed there were all types of indications for hysterectomy, both benign and malignant disease. There were 170 abdominal and 83 vaginal hysterectomies. Results were good in both.

The author presents his series of cases as a plea for more general use of complete hysterectomies. It is thought that the incidence of carcinoma of the cervical stump is about 4 per cent. Moreover, the cervical stump is particularly susceptible to chronic cervicitis.

Four cases of carcinoma of the cervix were discovered histologically in a routine examination of all removed cervixes in this series. In these 4 cases the hysterectomy was performed for benign disease of the fundus.

The operative mortality of this series was not any higher than the subtotal operation and was lower than the incidence of carcinoma of the cervical stump. Frequent injury to the ureter and bladder will not occur if the peritoneal folds of the broad ligament are incised freely, the bladder mobilized, and if the surgeon visualizes what is in the grasp of each hemostat.

The vagina will not be shortened if an anatomical incision is carried out and if no more than the cervix is excised. The vaginal vault will not prolapse if the round, utero-sacral and cardinal ligaments are incorporated into the angle of the vaginal cuff under normal tension.

With training and experience a surgeon can develop a technique in which total hysterectomy can be performed as safely as the subtotal operation. If the cervix is removed, it cannot become infected, degenerate, prolapse or become malignant.

(The long debate between the subtotal and the total hysterectomists appears to have drawn to a close and I believe that any dispassionate person would decide that the advocates of the total technic have been clearly left in possession of the field. This is not to say that there are not still a good many dissenters, nor does it mean that no qualifying strings are attached to the popular trend. I believe that total hysterectomy should always be done unless the technical difficulties and hazards presented by the particular case are sufficiently forbidding to more than counterbalance the real desirability of removing the cervix. This particular stipulation includes consideration of the operator's experience with the total procedure. In spite of what many say to the contrary, it is often a good deal harder than the subtotal, and in the hands of the occasional operator it seems foolish to argue that the hazard of injuring the bladder or ureter is not greater. The well-trained surgeon, however, can justly maintain that in a very large proportion of cases he finds it about as easy as a subtotal operation, with very little risk of injury to the bladder or ureters. I always approach a hysterectomy prejudiced toward doing the total procedure, but I hope the time

will never come when I do not have sense enough to compromise for the subtotal—because I believe it is a compromise—if the cervix is solidly fixed low down in the deep pelvis of a fat woman, with perhaps extensive adhesions welding the uterus and cervix to the rectum, to mention only one of the contraindicating pictures. To insist on doing a pan-hysterectomy under such conditions is to practice with a vengeance the vicious policy of fitting the patient to the operation, and imposing a hazard definitely greater under such circumstances than that of retaining the cervix, undesirable though the latter may be. On the basis of such concepts, I suppose that at least 80 per cent of my hysterectomies are of the total variety.

The objection of shortening the vagina, with subsequent dyspareunia, has never impressed me as a very important one. I do not believe that the vagina is materially shortened in most total hysterectomies except of course those for cancer. I do believe, however, that some patients do complain of dyspareunia, which has always seemed to me to be due less to vaginal shortening than to the tenderness of the scar in the vaginal vault. Rarely, however, has the difficulty been a serious one, and it is often only temporary. There are many other pros and cons concerning this question, but I have the impression that the majority of experienced gynecologists are guided by somewhat the same general principles as I have mentioned above.—Ed.)

STERILITY

WHY STERILITY?

S. L. SIEGLER

Brooklyn, New York

Urol. & Cutan. Rev., 52: 571-575, (Oct.) 1948

The writer notes that it is conservatively estimated that there are about 1,500,000 childless married couples in the United States who want children, and that the male is to blame in at least one out of every 3 infertile matings. The changes which modern civilization has made in the ambitions and living habits of women sometimes help to impair her fertility. However, the inherent desire for motherhood in every woman makes sterility a psychological problem in many such cases. Sterility therefore becomes both an individual and a social problem.

The importance of early investigation of infertility problems is stressed.

The essential factors for a fertile mating are outlined and the causative factors of sterility are discussed. The tubal factor precedes every other factor in importance as the cause of infertility.

The following steps are recommended as a basic scheme of investigation of essential factors in the study of sterility:

1. Complete history and physical examination of husband and wife, including laboratory data.
2. Evaluation of semen.
3. Evaluation of cervical factor.
4. Evaluation of tubal factor.
5. Determination of ovulation and so-called "fertile period."
6. Evaluation of factors found.
7. Fertility index and prognosis.
8. Recommendations.
9. Conference with couple.

Thoroughness of investigation should be an inflexible rule before any treatment is attempted. The indiscriminate use of both artificial insemination and glandular therapy should be forcefully condemned. The factors found in both marriage partners should be treated simultaneously.

(See comment below, on abstract of paper by Haman.—Ed.)

will never come when I do not have sense enough to compromise for the subtotal—because I believe it is a compromise—if the cervix is solidly fixed low down in the deep pelvis of a fat woman, with perhaps extensive adhesions welding the uterus and cervix to the rectum, to mention only one of the contraindicating pictures. To insist on doing a pan-hysterectomy under such conditions is to practice with a vengeance the vicious policy of fitting the patient to the operation, and imposing a hazard definitely greater under such circumstances than that of retaining the cervix, undesirable though the latter may be. On the basis of such concepts, I suppose that at least 80 per cent of my hysterectomies are of the total variety.

The objection of shortening the vagina, with subsequent dyspareunia, has never impressed me as a very important one. I do not believe that the vagina is materially shortened in most total hysterectomies except of course those for cancer. I do believe, however, that some patients do complain of dyspareunia, which has always seemed to me to be due less to vaginal shortening than to the tenderness of the scar in the vaginal vault. Rarely, however, has the difficulty been a serious one, and it is often only temporary. There are many other pros and cons concerning this question, but I have the impression that the majority of experienced gynecologists are guided by somewhat the same general principles as I have mentioned above.—Ed.)

THE PRESSURE-TREATMENT OF BLOCKED FALLOPIAN TUBES

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Urol. & Cutan. Rev., 52: 575-577, (Oct.) 1948

The writers have treated 124 patients (unselected except for exclusion of those with pelvic masses or subacute sepsis) suffering from blocked fallopian tubes. The criterion for a diagnosis of blocked tubes was that the tubes be impermeable to gas after several attempts at one sitting, and also that they be proved impermeable to oil at a separate and subsequent test. Treatment consisted first of utero-tubal insufflation with carbon dioxide, administered with a flow at 64 cc. per minute up to a pressure of 250 mm. Hg. Two such insufflations were given 10 to 12 days after conclusion of menstruation in separate months. A third test was made one month later. Oil was injected at a pressure of 250 to 300 mm. Hg, an x-ray was taken at the time, and another plain x-ray 2 days later.

Of the 124 patients treated, 53 developed satisfactory tubal patency and a further 9 progressed from total blockage to tubal stenosis. The number of pregnancies has been 23 to date (1 in 5.4), of which there were 2 ectopic gestations and 3 miscarriages. No fatalities were experienced. With a selected group of patients, much more favorable results are expected in the future.

(See comment below, on abstract of paper by Haman.—Ed.)

TUBAL PATENCY TESTS

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Urol. & Cutan. Rev., 52: 582-584, (Oct.) 1948

Determination of the tubal status is a very important factor in studying sterility cases. Uterotubal insufflation and hysterosalpingography have become widely accepted as methods of determining tubal patency. Before using these tests in any case, one must be certain that no contraindications exist, such as infection of the genital tract. The proper time for testing is during the week following menstruation.

Modern insufflation equipment employs carbon dioxide and includes a kymograph so that pressure changes can be accurately ascertained and recorded. The use of air is needlessly dangerous.

In cases presenting doubtful results upon insufflation and in those presenting

NEWER ASPECTS OF STERILITY

M. J. WHITELAW

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Arizona Med., 5: 25-32, (Nov.) 1948

The author emphasizes that every barren marriage must be treated as a unit, with both members undergoing a complete examination. This examination must entail not only a painstaking and accurate anamnesis based upon newer knowledge of the various causes of sterility, but also a careful physical examination and full utilization of laboratory tests where indicated. It has become increasingly evident that the preventive aspect of sterility will occupy an even greater role. Genital underdevelopment must be treated early and infectious causes of sterility can now be better controlled with the antibiotic drugs.

Any surgical procedure involving the genital organs should follow conservative lines whenever possible during the childbearing period and conservation of function should be its goal. Basal temperature graphs and vaginal and cervical smears are of value in determining the exact time of ovulation. The knowledge of this time is of major importance in any particular case study. In the future, it may be possible to induce ovulation at the opportune time with the use of purified hormonal substances.

Inasmuch as nidation normally has to take place in the tubes, these must be intact physiologically and anatomically. The use of radio-opaque substances and of uterotubal insufflation is of value in determining tubal patency. Endometrial biopsy at the time of menstruation is often of diagnostic value and may point to specific courses to be taken. The use of the culdoscope offers a method of direct visualization of the tubes, ovaries and uterus.

The male should not be neglected in any study of sterility, as about 50 per cent of such cases are directly traceable to the male partner. Sperm counts and analysis should be performed. Azoospermia may be due to defective production or to complete obstruction of the passage-ways. Reconstructive surgery in the latter cases has proved of benefit in certain instances. In cases of azoospermia where there is doubt as to the etiology, a testicular biopsy should be performed. The role and possible future uses of hyaluronidase in sterility are still under question, although so far, application of this substance to the cervix has been disappointing. Artificial insemination has been used successfully in many instances. 8 figures.

(See comment below, on abstract of paper by Haman.—Ed.)

both somatic and sexual, and due attention given to faulty habits or general hygiene that may alter fertility.

(See comment below, on abstract of paper by Haman.—Ed.)

NUMBER OF SPERMS REQUIRED FOR FERTILIZATION

C. R. AUSTIN

National Institute for Medical Research, London

Nature, 162: 534-535, (Oct. 2) 1948

There have been markedly divergent views as to the number of sperms normally present in the immediate vicinity of the egg at fertilization. On the one hand, such direct evidence as exists suggests that very small numbers are present. On the other hand, it is a widely held theory that the egg must be freed from the surrounding mass of follicular cells, by means of hyaluronidase before sperm penetration can take place, and there is a strong implication that a large aggregation of sperms is necessary to assure an adequate concentration of hyaluronidase. However, it has been shown in rats and in rabbits that denudation of the egg is not always a prerequisite for fertilization.

The author has carried out insemination of rats and rabbits, and sperm counts were then made from the tubes of these animals. On the basis of these observations, it was concluded that fertilization can take place where there are in the vicinity of the egg less than 100 sperms in the rat, and less than 1000 in the rabbit.

(See comment below, on abstract of paper by Haman.—Ed.)

ARTIFICIAL INSEMINATION: ITS POSITION IN THE TREATMENT OF STERILITY

J. O. HAMAN

San Francisco, California

Urol. & Cutan. Rev., 52: 569-571, (Oct.) 1948

The prerequisites which must be fulfilled before performing artificial insemination are: (1) the husband must be azoospermic or so nearly so that after adequate and prolonged treatment his chances of impregnating his wife are very small; (2) his wife must have normal pelvic organs and must produce normal ova in a great majority of her cycles; and (3) the couple must realize the possible psychological and legal consequences that the procedure presents.

definite evidence of tubal non-patency, hysterosalpingography should be employed.

Negative or doubtful results with either test indicate the necessity for repetition of the investigation and supplementary employment of the other procedure. Repeated checks are advised before subjecting a patient to laparotomy for reconstruction operations upon the salpinges.

(See comment below, on abstract of paper by Haman.—Ed.)

THE EVALUATION OF MALE INFERTILITY

W. W. WILLIAMS

Springfield Hospital, New York City

Urol. & Cutan. Rev., 52: 577-582, (Oct.) 1948

Treatment of male sterility, to be most effective, must be based on a comprehensive knowledge of the various underlying factors which may affect the fertility of either sex. In various respects, male sterility cannot be dissociated from that of the female, and its study should be part of the comprehensive study of the infertile couple. It is highly desirable that semen examination should precede studies and therapy to the wife.

Comprehensive semen examination is the most important element of the male diagnostic survey, and will reveal the cause of sterility in a greater ratio of cases than any other single test unless it be the Rubin test applied in communities where pelvic inflammatory disease is prevalent.

The diagnostic survey of the male should include as a minimum:

1. A comprehensive anamnesis.
2. General physical examination.
3. Examination of generative organs, including accessory glands.
4. Semen examination.
 - (a) Sperm density.
 - (b) Motility and duration of motility.
 - (c) Examination of a properly stained semen smear, including type and number of spermatocidal abnormalities.

Semen volume or sperm concentration, except when exceedingly low, have little effect on fertilization per se, but together are often a part of the picture of severe spermatocidal disease. Impaired motility indicates lessened sperm vitality. The prognosis is much worse if a low motility is associated with a high incidence of defective sperms. The prognosis is very poor or hopeless when a high ratio of pathologic sperms (40 to 50 per cent) is present in a numerically depleted population.

Any therapy should be outlined on the basis of known pathology present,

THE ADVANTAGES OF HYSTEOSALPINGOGRAPHY UNDER FLUOROSCOPIC CONTROL

D. W. GOLDMAN

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Urol. & Cutan. Rev., 52: 606-607, (Oct.) 1948

The author presents a detailed simplified technique for hysterosalpingography under fluoroscopic control. The advantages are reemphasized and a wider application of this safer and more informative procedure is urged on all sterility investigators.

The technique concerns itself specifically with the replacement of x-ray films of the pelvis in uterosalpingography by direct visualization by means of fluoroscopy. Fluoroscopic control allows placing the patient in both oblique positions for observation. Also, there is eliminated the confusion in interpretation when the uterine shadow lies over the tubal shadows.

The author feels that the routine use of antispasmodics is desirable to overcome uterotubal spasm. The routine administration of one of the histamine antagonists just prior to the test is advised. An aqueous opaque solution is deemed safer as a contrast medium than lipiodol. Fractional amounts of opaque medium are injected at the outset of the test so that immediate observation may be made as to abnormalities in contour of the uterine cavity. The injection is then continued until all necessary information is obtained. Spot films are taken at intervals to note the progress of filling and any pertinent abnormalities.

SURGERY IN THE TREATMENT OF STERILITY

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Urol. & Cutan. Rev., 52: 586-590, (Oct.) 1948

Surgery for the relief of sterility is considered after a complete history is taken and a thorough physical examination is performed. All other means of treatment must have failed. Before surgery is done, the patient's cause for the sterility is checked by proper laboratory workup, including blood, urine, blood sedimentation, Rh factor, uterotubal insufflation and uterosalpingography. While too high a hope should not be held out to these individuals, with careful technique and the application of the basic principles involved, the percentage may be increased. In the event that there is blockage of the fallopian tubes

Artificial insemination was performed on 82 women, 47 with donor's semen and 35 with husband's semen. Of these, 48.7 per cent became pregnant, 66.1 per cent by the use of a donor and 28.5 per cent by the use of the husband's semen. Insemination was performed an average of 2.7 times per cycle. Of the successful inseminations, 42.5 per cent occurred within 3 months.

Artificial insemination is suggested as one possible solution to the problem of present population trends, to provide for a stable population and assist in improving the health, physical and mental strength of its children. The fact that frustration as to motherhood may have great bearing on the mental and physical well-being of women can in itself be regarded as a therapeutic indication for artificial insemination.

The legal status of artificial insemination is discussed, and it is concluded that to obtain statutory clarification of the rights of persons in a new field such as this, there must be established customs which are generally considered morally sound. This involves careful practice on the part of physicians and dissemination of information as to the benefits of the treatment.

(The foregoing papers deal with various aspects of both female and male infertility. While they bring out new points, they are all conservatively written and emphasize well-accepted principles. The scheme of investigation suggested by Siegler has the virtue of simplicity combined with reasonable comprehensiveness, which is not true of some of the over-elaborate rituals outlined by some authors.

Somewhat the same statement may be made of Whitelaw's paper. Most of us, however, will probably feel that his estimate of 50 per cent for the responsibility of the male is a bit too high, and that Siegler's figure of $\frac{1}{3}$ of all cases is more nearly correct. Many, also, will share his doubt as to whether the clinical employment of hyaluronidase will yield worthwhile results, and the studies reported in Austin's paper likewise furnish at least some laboratory evidence to justify such skepticism. These studies lead him to the conclusion that fertilization can occur, at least in the rat, even though the egg is not surrounded by the swarms of spermatozoa which some have thought necessary to the production of sufficient hyaluronidase to denude the egg. In fact, he concludes that such denudation is not a prerequisite for fertilization.

The paper of the Beachams is a satisfactory short resumé of tubal patency tests. Grant and Mackey's employment of pressures of 250 mm. in carbon dioxide would seem not without hazard, as tubes have been ruptured at lower pressures than this. A safer maximum is 200 mm. and I believe that this is the one most generally accepted. He recommends doing the insufflation 10 to 12 days after the cessation of menstruation, which in most cases would be after the occurrence of ovulation. This would seem to carry with it the hazard of occasionally blowing out an unimplanted fertilized egg. My own preference is for about the 9th day of the cycle, just before the usual optimum period for conception in women with approximately 4-week cycles.

Williams, who has given much attention to the study of semen, reviews the seminal factor in male infertility briefly and satisfactorily, while Haman exhibits at least a moderate degree of enthusiasm for the employment of artificial insemination when proper indications are present. The bugbear in the minds of most physicians is the legal aspect, especially as there is so much variance and vagueness in the laws of the various states. This would be too big and too technical a question to embark on here. Most gynecologists probably look upon the procedure as a rather messy and subterranean one. In most good-sized communities there are likely to be a few enthusiasts for the method, and the average gynecologist is only too glad to refer to these the occasional case in which insemination is apparently indicated and is desired by both husband and wife.—Ed.)

eggs are usually unripe when discharged from the ovary, so that they cannot take the spermatozoal fertilizing charge. However, in rare cases maturation appears to be completed in the ovary, as attested by the occasional cases of ovarian pregnancy. In general, maturation is completed in the outer portion of the tube, and in the absence of the latter, fertilization must be rare.

■ To summarize, therefore, no one is justified in performing operations of any of the above types unless the patient and her husband understand the slimness of the chances of success. When such an explanation is given, the majority of couples will prefer adoption to operation, especially when the wife has no symptoms referable to her pelvic disease. On the other hand, there are women who will willingly or even eagerly submit to operation, no matter how pessimistically the outlook is painted, if the surgeon can tell them, as he honestly can, that there is at least a slim chance of success. Under such circumstances I believe that such operations are justified.

It is my impression that the psychology of patients of this type is that they feel that they have done all that they can to accomplish the desired result. If the miracle happens they are of course happy. If not, they feel they have done their "darndest." It is not a bad plan, since the surgeon himself does not usually feel overly enthusiastic over the result of his operation, to suggest that the patient adopt a baby pending results. This will give her a family nest egg in the meantime and afford an outlet for her maternal craving, with no disadvantage should an unexpected baby of her own come along later.—Ed.)

THE USE OF VAGINAL SMEARS IN THE STUDY OF STERILITY

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Urol. & Cutan. Rev., 52: 590-591, (Oct.) 1948

The writer concludes that the vaginal smear is valuable as an aid in the study of sterile couples from the standpoint of estrogen function and ovulation. The evidence it gives is valuable chiefly from a positive standpoint, negative findings being less reliable. When attempting to determine the occurrence of ovulation by such means, a series of successive smears will show whether or not ovulation takes place, whereas a single smear yields no degree of accuracy. In cases of ovarian failure the smear shows accurately the level of estrogen secretion and compares well with the endometrial biopsy. The smear can be further utilized to follow the course of therapy.

The smear should not be used to supplant other methods, but should function as an adjuvant to them. It must be emphasized that the value of the method increases in direct proportion to the skill of the examiner and the number of slides studied in the particular case.

(Personally I just don't believe that vaginal smears for the purpose described by the author are comparable to a single premenstrual biopsy in the information which they yield, not only as to the occurrence of ovulation, but also as to the response of the particular endometrium to both estrogen and progesterone. When the biopsy is done premenstrually, it is wise to counsel avoidance of coitus before the usual ovulation span, to avoid the possibility of disturbing a possible early implantation. It is also important to have the patient note

in the female, or the seminal ducts in the male, surgery is the only hope that may be held out for the relief of sterility.

The author discusses vaginal, cervical, uterine, ovarian and tubal surgery in sterility. The indications and contraindications for tubal surgery are set forth. The general considerations in tubal surgery include care in selecting the portion of tube to be operated. This should not be too near the cornua, since the lumen is smallest at this point. Gauze should be employed in holding the tube during surgery. Tubal implantation into the uterus is the best method of surgery in block of the lumen unless the fimbria is the cause of closure. Great care should be taken to maintain and preserve the vascular supply, fine suture material should be used, and the greatest care taken to avoid distortion and conserve the anatomy as nearly to normal as possible. The results of tubal surgery have been variable. Of 16 cases operated by the author, 6 pregnancies have resulted (37.5 per cent), with an incidence of abortion of 16.66 per cent and no ectopic pregnancies. Failure of tubal surgery is usually due to end-to-end anastomoses at the narrow portion, unselected cases, improper handling of the tubes, using too many sutures, not inserting the tube well into the uterus, or not giving penicillin postoperatively.

(The author of this paper must just about have used up his luck in obtaining 37.5 per cent of pregnancies in his 16 cases of tubouterine anastomosis, with no ectopic pregnancies among them. Were the results reported by others in conformity with this experience, there would be far more justification for a frequent resort to such plastic procedures than there is. A more common estimate for the incidence of successes is something like 5 per cent, but it is probable that even this is too high. The failures are rarely reported, but the successes are likely to be.

I cannot conceive that anyone would try to do an end-to-end anastomosis at the narrowest part of the tube, against which the author warns. Anyone who has done plastic tubal surgery would feel that such attempts are foreordained to failure. Even the usual type of uterotubal anastomosis, in which the minutely narrow and often completely obliterated inner portion of the tube is resected and the wider outer portion utilized, is a very imperfect procedure, regardless of who does it and how precise his technic. There can never be the accurate layer-to-layer approximation possible in intestinal anastomosis. The tubal segment is simply drawn into the uterus and I agree that it should be well drawn in to allow for probable retraction, so that the tubal and uterine mucous membranes, it is hoped, will be reasonably close. The regenerative and proliferative capacity of the endometrium must be depended upon to fill in the gap and maintain a patent canal. The insufflations which should always be done postoperatively, as well as the subsequent histories of these patients, have shown how often the hopes for maintaining such patency are not realized.

The cases in which, at operation, reverse insufflation shows the inner portion of the tube to be patent, while the fimbriated orifice is closed and bulbous, appear to be somewhat more hopeful and technically easier, and all sorts of technics have been devised to maintain the patency of the tubal orifice. Even in this group no one can consider the results anything to cheer about.

In a third group of cases, in which the tubes are hopelessly damaged or perhaps have been previously removed, the only procedure to consider would be some type of cornual implantation of the ovary, whether by the Estes or Tuffier procedures, or some compromise method. Among the latter, the most nearly sensible is to suture the ovary into a very deep cornuectomy wound so that its convexity abuts into the uterine cavity, in the hope that the patient will "lay" her eggs into the latter. This sounds very nice, but the hitch is that these

THE DIAGNOSIS AND TREATMENT OF THE ENDOCRINE
FACTORS IN FEMALE STERILITY

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Urol. & Cutan. Rev., 52: 603-606, (Oct.) 1948

The most common cause of amenorrhea with associated infertility is the Frölich type of functional pituitary deficiency. In about 20 per cent of amenorrheal, infertile patients, one may find clinical and laboratory evidence of primary ovarian deficiency. Both amenorrhea and menometrorrhagia of thyroid origin reduce fertility.

In the treatment of amenorrhea and associated infertility, one must first eliminate the possible existence of an organic lesion of the pelvic organs and pituitary gland. The thyroid type of amenorrhea requires regulation of the basal metabolic rate to a plus 5 per cent. Cyclic estrogen-progestin treatment restores the menstrual rhythm and fertility in about 15 per cent of patients with amenorrhea and associated infertility. For those with polycystic ovaries, Stein successfully employs bilateral removal of a wedge of ovary to reduce intraovarian tension.

The most effective, quickest and least expensive method of restoring menstrual rhythm and fertility is low-dosage irradiation of the pituitary gland and ovaries. This treatment of 57 infertile women in whom amenorrhea was the sole cause is presented in this paper. Forty-three, or 75.4 per cent of these women conceived after the first, second or third cyclic flow following treatment. Thirty-eight of the 43 women delivered healthy infants. Permanent restoration of menstrual rhythm was achieved in 88 per cent of the 43 women.

Menorrhagia of endocrine origin is usually caused by a functionally defective corpus luteum. If a deficient corpus luteum influence is diagnosed, treatment with chorionic gonadotrophin usually yields excellent results. Metrorrhagia in infertile women is usually caused by organic pelvic lesions. In the absence of such lesions, curettage and chorionic gonadotrophin therapy usually correct the metrorrhagia.

The diagnosis of anovular menstruation as a cause of infertility is limited to the following 3 methods: (1) premenstrual biopsy or curettage of the uterus; (2) cyclic fluctuation in the basal body temperature; and (3) the 2-hour rat test of Farris. When anovular menstruation is associated with oligomenorrhea, low-dosage irradiation of the pituitary gland and ovaries usually restores the menstrual rhythm and evokes ovulation. Equine gonadotrophin or Synapoidin therapy produced ovulatory cycles in about half of the authors' patients. Small doses of desiccated thyroid tissue, a balanced diet and elimination of emotional conflicts are equally important in the treatment of anovular menstruation and associated infertility.

(The senior author of this paper, next to Kaplan, has been perhaps the warmest advocate of low-dosage irradiation of the pituitary gland and ovaries in many cases of amenorrhea

the exact date of the menstrual flow following the biopsy to permit of more intelligent evaluation of the findings, especially if the menstrual intervals are somewhat irregular. With these precautions, I have come to believe that premenstrual biopsy is preferable to biopsy shortly after the menstrual onset, in which the tissue is often so degenerated and autolyzed as to make histological evaluation rather difficult. Vaginal smears give a good idea as to the vaginal response to estrogen, but far less satisfactory information concerning progesterone effect.—Ed.)

OVULATION TIMING BY BASAL BODY TEMPERATURE CURVES

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Urol. & Cutan. Rev., 52: 596-600, (Oct.) 1948

The author concludes that basal body temperatures are reliable depending upon the accuracy of the patient and the accurate interpretation of the examiner in establishing the time of ovulation. The curves may emphatically illustrate lack of ovulation, a poor ovulation, or delayed progestational effect. Added value of basal temperatures may be derived in regard to diagnosing pregnancy, and in creating a reliable graphic rhythm contraceptive calendar. The graphs are an inexpensive aid to the diagnostic armamentarium of the gynecologist and sterility specialist, and only 5 minutes of actual timing is necessary for the average intelligent patient to be instructed in the technique. Nine illustrative charts are presented from the author's experience which show various conditions and types of graphs.

Standardization of technique and interpretation is needed and more care in instructing the patient and examiner in their reading and interpretation. Added value will derive from study of associated endometrium secured at stated dates in the menstrual cycle as predicted by these graphs.

(Basal temperature studies have usually been recommended in the management of sterility patients, and not as a help to those anxious to avoid pregnancy. I presume that the author's suggestion of utilizing basal temperatures as a basis for a "reliable graphic rhythm contraceptive calendar" is meant to apply to patients whose religious convictions exclude the use of mechanical and chemical contraceptive measures. If the latter considerations are not involved, there is no question in my own mind as to the superiority and greater efficacy of the chemical and mechanical devices.

The whole question of basal temperatures in the management of sterility patients has been discussed many times in these pages. My own feeling is that the chief field for such studies is in women with very irregular cycles. In those with reasonably regular cycles, optimum periods for conception have long been established, so that patients can be advised as to the importance of frequent coitus during those periods. Not much more advantage accrues from determining the date of temperature rise by basal temperatures, which not a few women find distasteful, aside from certain pitfalls in interpretation. Moreover, the exact chronological relation between the actual extrusion of the egg from the ovary and the temperature rise is still a matter of some doubt.—Ed.)

porters of this plan of treatment. The chief objection urged against it has been the uncertainty as to possible serious effects, not so much on the mother or her immediate offspring, but upon succeeding generations. As far as I know there is as yet no worthwhile available evidence on the latter point in humans, so that we cannot yet know whether a succeeding generation will show any of the somatic mutation effects which Little and other genetists have shown to occur in the third generation of similarly radiated laboratory animals. Kaplan's follow-up report deals only with the mothers and their immediate offspring.—Ed.)

TERMINOLOGY OF SPERM PATHOLOGY

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Urol. & Cutan. Rev., 52: 592-595, (Oct.) 1948

The existing confusion in terminology in the field of sterility is especially marked when it comes to semen studies. The author presents, in this paper, suggestions for standard nomenclature, and describes the variations found in sperm analysis.

Ejaculate is the material ejected from the male urethra, and semen is ejaculate containing male germ cells. Seminal fluid is the liquid component of semen and seminal cells the cellular elements of semen. Spermatopoiesis refers to germ cell production and spermatogenesis to spermatozoa production.

All the cells of the spermatogenesis series are seen on histologic examination of a normal testicle. In stained films of normal semen one finds predominantly spermatozoa. Normally, only from 0.25 to 2 per cent of immature cells, mostly spermatids, are found. Those who tabulate only spermatozoa and not their precursors miss evidence of regeneration of the germ tissue and fail to diagnose maturation arrest and its degree from semen films, thereby having to resort to testicular biopsy for this purpose.

Terms are listed to apply to semen findings in respect to the predominant cell type, e.g., normozoospermia: normal sperms, or microzoospermia: sperms with small heads. Besides immature and mature, normal and abnormal cells of the spermatogenesis series, other elements may be seen on occasion (pyospermia: semen mixed with pus, or hemospermia: semen mixed with blood).

Terms are listed to describe the degree of motility, as normokinesis: normal motility, or oligokinesis: sluggish motility.

The prefix "zoo" is very convenient where one intends to differentiate between conditions pertaining to the sperms only and not to the ejaculate as a whole. For instance, normospermia signifies normal semen, whereas normozoospermia denotes normal spermatozoa; and hypospermia signifies very deficient semen, whereas hypozoospermia means very deficient spermatozoa.

The author suggests that the terms and classification offered in this paper

and sterility. A comment on this point is appended to the abstract of Kaplan's paper, immediately following this. If the results which the present authors report could be obtained by others in cases not amenable to other less debatable plans of treatment, and if it were absolutely certain that no harm is done to later generations, x-ray therapy would be far more widely accepted than it has been. This does not mean that its employment is a matter of culpability, for it is used by many excellent gynecologists, but in a much smaller proportion of cases than by Kaplan and Mazer.

The authors are more optimistic than most others in their belief that "chorionic gonadotrophin usually yields excellent results" in functional menorrhagia.

It is undoubtedly helpful in some of the more moderate cases, but it appears to have much less vogue than it did 15 years ago. I can speak feelingly on this point, because one of the earliest reports on this form of hormone therapy was that of Novak and Hurd in 1932. This was before progesterone had become clinically available, or before the days of testosterone, and of course long before the utilization of estrogens or so-called cyclic plans. Since no plan even yet approaches the ideal, I find it difficult to criticize the other fellow's ideas and methods on this point unless they are obviously or glaringly irrational. I do, believe, however, that the chorionic gonadotrophic hormones have been discarded by the majority of gynecologists in favor of some of the more modern fashions in endocrine therapy.

Finally, of the 3 methods mentioned for the diagnosis of anovulatory menstruation, it is only the first which, to my mind, need be considered as both easily practicable and quite reliable. This can certainly not be said of either the second or the third.—Ed.)

EFFECTS OF RADIATION ON GERM PLASM

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Urol. & Cutan. Rev., 52: 608, (Oct.) 1948

The various theories related to the possible action of x-rays in the therapeutics of sterility are discussed. Cases are cited in detail illustrating the suggested explanations of the workings of irradiation. The technic employed in treating sterile women by x-rays is described.

Of 402 cases of married women treated by irradiation, 307 have been followed up. Of these, 95 failed to respond to treatment and 242 had menstruation regulated. Of these, 118 became pregnant, 98 went to term, 22 more than once, and gave birth to 125 normal living children. There were 32 pregnancies without living children; of these, 2 were ectopics, 1 a stillbirth, 1 an abnormal child, 3 children died immediately after birth and there was 1 therapeutic abortion following irradiation. At present, 6 women are still pregnant.

The results bear out the author's contention that irradiation, when properly given, is harmful neither to the mother nor to the offspring, and that it has proved a valuable therapeutic procedure for the treatment of amenorrhea and relief of sterility.

(The subject of radiation therapy for amenorrhea and sterility has been frequently discussed in these pages. The author of the above paper is one of the most enthusiastic sup-

MISCELLANEOUS

THE VALUE OF CONSERVATIVE SURGERY OF THE PELVIC ORGANS

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Am. Practitioner, 3: 34-36, (Sept.) 1948

Needless or ill-advised surgery of the female pelvic organs often gives rise to serious physiologic and psychologic trauma and causes irreparable damage to the patient. The removal of one ovary may be responsible for menstrual irregularities and premature menopause, and if part of the remaining ovary is also removed, a normal cycle is virtually impossible. The anovulatory cycles which often result from such operations may give rise to functional uterine bleeding. The hormonal balance is disrupted and estrogen deficiencies may occur. On the other hand, with the estrogenic substances available for replacement therapy, if radical surgery is indicated, no diseased ovarian tissue should be allowed to remain. If it does become necessary to remove both ovaries, it is usually wise also to remove the fundus, in order that functional bleeding may be avoided.

In regard to endometriosis, the author feels that many patients may be materially improved or even cured by surgery when it is done in the early stages of the disease. Surgery in such cases is often difficult but may be rewarded by a successful pregnancy. If pain does persist, the disease may then be arrested by irradiation.

Conservation of the uterus is often forgotten and an unnecessary hysterectomy is performed. Too often the patient who complains of uterine bleeding is so operated, only to discover later that there is a carcinoma present in the cervix; or the patient with functional bleeding, who insists that she will never marry, returns in several years, married and desirous of children. Every surgeon should ask himself before he does a hysterectomy, "Would I want one done on my mother, wife or daughter for this condition?"

(The author's plea for a generally conservative policy in gynecological surgery admits of very little difference of opinion, although everyone knows that large numbers of essentially normal ovaries and uteri are needlessly sacrificed each year. As to his statement that removal of one ovary and part of the other renders normal cycles virtually impossible, I believe there are many exceptions both as to menstruation and ovulation, the latter being attested by the subsequent occurrence of pregnancy. This applies especially to cases in which only a comparatively small fraction of the conserved ovary has been removed.

In connection with conservation of the ovaries, one can easily elicit a sharp division of opinion among surgeons as to whether or not one or both ovaries should be conserved when hysterectomy is necessary for benign lesions, such as large myomas, in women at the menopausal or immediately premenopausal age. There are some who believe that ovarian tissue

should prove valuable in seminal terminology and in the field of sterility as a whole if accepted as a common denominator.

(The terminology suggested by the author is a rational one, and the majority of the designations which he suggests are in common usage. Systems of nomenclature, however rational they may be, are rarely adopted bodily or universally, nor will this one be. In such things the way of the reformer is indeed a hard and discouraging one.—Ed.)

TREATMENT OF STERILITY: INSEMINATION TIMED BY RAT OVULATION TEST

REPORT OF THIRTY-TWO CASES

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J. A. M. A., 138: 13-14, (Sept. 4) 1948

This paper deals with the use of the rat ovulation test to predict the day for insemination of a series of 32 women. The patients represented a selected group of infertile couples who had been treated unsuccessfully by others. In many cases the husband had a low sperm count and the wife's ovulation reaction was unsatisfactory; the insemination was carried out reluctantly in these cases, on the insistence of the couples concerned.

Fifty-seven inseminations were performed on the 32 women. Ten resulted in conception, 8 of the 10 women conceiving as a result of the first treatment, and the remaining 2 conceiving after their second inseminations. Of the 47 inseminations which failed in their objective, 37 (79 per cent) were charged to either an inadequate number of moving sperm cells or abnormal ovulation. Each of the failures in these 2 categories was predicted before the insemination was performed. The fact that 8 of the 10 conceptions occurred on the first insemination seemed to speak well for the accuracy of the rat ovulation test as a method of determining the day when an egg is available for fertilization. When the failures are excluded which were predicted before insemination, it would appear that conception was achieved in an extremely high percentage of cases.

Maladjustment to children appeared secondary to that with the husband. Of the 56 patients maladjusted to their husbands, 53 per cent did not experience orgasm and 26.8 per cent complained of dyspareunia which seemed to represent resentment against the husband and in some cases fear of becoming pregnant.

Sexual frustration and fear of pregnancy were often associated in those women with normal sexual impulses who rarely or never experienced orgasm. Here unsatisfactory contraceptive measures were often used. Abdominal pain and sexual frustration were also combined. The symptoms of dysmenorrhea of the congestive type, severe "middle pain" or continuous dragging pain were not connected with gross pathology often and could not be eradicated easily. In a few cases hysterectomy was necessary in order to leave the woman able to deal with her problems. The uterus was a symbol of danger and uncertainty which the women needed to eradicate.

In 33 cases emotional immaturity was so great that the patients were incapable of adapting to marriage. The symptoms most complained of by this group were frigidity, dyspareunia, dysmenorrhea, vaginal discharge, non-consummation and infertility. The physical findings were hypoplasia and some infective vaginal discharge.

Infertility was a prime factor in 27 of those cases complaining of absence of orgasm and dyspareunia. Fear of disease figured in the neurosis of 16 patients. Housing problems, separation from husband, and inadequate social outlets were contributing factors in many cases.

Short term therapy was attempted in 84 cases with an average of 7 interviews per week for 15 weeks. Where the husband was involved he was asked to attend a special Sunday morning clinic. Treatment was confined to exploration, re-education and reassurance, with no special emphasis placed on the psychological nature of the treatment.

A weekly contraceptive clinic, social welfare measures, minor treatment of such things as a *Trichomonas* infection were supplementary measures. In some cases surgical sterilization was necessary.

(The organized effort described by the authors to study the psychiatric aspects of the problems presented by gynecological patients is evidence of the growing recognition of both the frequency and importance of this relationship. Not only in gynecology, but in all other fields of practice, the psychosomatic aspects, to use a term which bids fair to become hackneyed, are being stressed. The very great frequency of functional gastrointestinal disorders, and even of peptic ulcers, as a result of emotional factors, has long been recognized by gastroenterologists; and internists must envisage the psychosomatic factor in the evaluation of a whole array of symptoms, from headache to hyperthyroidism. Even in obstetrics, Grantley Read has made his colleagues think of the possible utilization of psychosomatic methods in the conduct of pregnancy and labor.

It is probable, however, that the gynecologist encounters the largest proportion of patients calling for evaluation of possible emotional factors, and a good many of these are discussed in the paper by Snaith and Ridley. One group not included in the above abstract, and a very important one, is represented by the rather heterogeneous group of women at or near the menopause, and presenting symptoms which may be genuinely menopausal, but which perhaps more often are not referable to the hormone changes characterizing that epoch. Not infrequently, they are middle life rather than menopausal in etiology, as in the

should be conserved even in women of 47 or 48, because they feel that a surgical menopause is likely to be harsher than the normal one. Some, indeed, have expressed the belief that the ovaries must have some function even after the menopause, although I know of no evidence to support this belief. Other gynecologists, and I number myself among these, believe that important and desirable as conservation of ovarian tissue is in the case of younger women, it is misdirected in the case of women at and after the menopausal era. They see no important difference between the natural menopause and that induced surgically at this epoch. Moreover, the relative frequency of cystadenomas, carcinomas and other tumors of the ovaries justifies the removal of the latter when they have already reached the end of their functional life.

Just what age line shall be drawn between the conservative and the radical plan will be answered somewhat differently by different gynecologists, nor need it necessarily be an arbitrary one. For example, in women of perhaps 42 or 43, I myself not infrequently remove one ovary, with the feeling that I am preserving an adequate endocrine function and at the same time dividing by two the woman's hazard of subsequent ovarian malignancy.

I agree with Allen that where removal of both ovaries is necessary, the uterus should likewise be removed, but not for fear of later functional bleeding, which could not occur in the absence of the ovaries. A residual uterus of this sort, however, would not only be a useless organ, but would remain a menace, not only from the standpoint of possible malignancy, but even more frequently because it may become fixed and adherent to the rectum and produce symptoms sometimes calling for later removal of the organ.

The Golden Rule question which Allen suggests to the prospective hysterectomist would be desirable for surgeons in all fields. If every surgeon asked himself this question before a contemplated operation, and answered it to himself honestly, the operating room schedules in all our hospitals would undergo considerable shrinkage.—Ed.)

GYNAECOLOGICAL PSYCHIATRY: A PRELIMINARY REPORT ON AN EXPERIMENTAL CLINIC

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Brit. M. J. 2: 418-421, (August 28) 1948

During the past 2 years there have been established facilities for psychiatric investigation and short term therapy within this gynecological clinic in order to avoid segregation and utilize the closest cooperation between the two fields. Patients who were victims of anxiety states with no physical cause of symptoms and those whose symptoms were not entirely compatible with physical findings were referred to the psychiatric unit.

In each case an attempt was made to assess the incidence and relative potency of etiological actors leading to the development of psychoneurotic disturbances and to correlate such factors with the somatic symptoms present. Of the 165 patients, 46 per cent were considered to possess psychologically unstable constitutions and to have less resistance to environmental and emotional stress.

Maladjustment to the husband was the commonest and most potent dynamic factor and was associated with faulty relationship with one or both parents.

2, metastases occurred in 5 patients who had had radiation. Of the 3 patients in stage 3 all were given radiation and one had metastases. Iliac, obturator and ureteric nodes were the most frequent sites of metastases. There was no operative mortality but shock was frequent and morbidity not so great as expected. The post-operative complications were probably due to interference with the blood and nerve supply.

The author prefers to treat carcinoma of the fundus with radium used at the time of diagnostic curettage, followed after 5 or 6 weeks by complete hysterectomy and bilateral salpingo-oophorectomy. However, individualization is the sheet anchor of treatment.

The incidence of ovarian malignancy is higher than fundal malignancy. The author urges investigational surgery where there is dermoid cyst, rapidly growing tumor, abscess, virilizing tumor or suspicious malignancy.

Most complications following therapy result from poor selection of risks, inadequate preparation and overtreatment. The X-ray is a destructive agent. If the full dosage can be given in the first attempt the effect is greater. Frequent follow-up of patients with various complications is obligatory.

In reevaluating the present status the author arrives at these conclusions. One member of the department should be responsible for all malignancy; scrupulous study and individualization of therapy are necessary as well as frequent checking on all patients. Cytologic smears are of value but should be checked by biopsy.

(A fair evaluation of the problem of gynecological cancer on the basis of a large material, expressing views which are in accordance with those generally held. Radical operation, including gland dissection, was done in 75 of the 530 patients, this group obviously including a good many Stage 2 cases in addition to the 51 of Stage 1. It is probably too early to evaluate this operative group and it will later be of interest to compare the 5 year results with those obtainable by irradiation in similar stages. It is apparent, not only from this report, but from those published by Meigs and others, that, thanks to transfusion, antibiotics and other surgical advances, these extensive operations can now be performed with an exceedingly low primary mortality. The need for individualization in the selection of methods of treatment cannot be too strongly emphasized.—Ed.)

ON COMPLICATIONS FOLLOWING THE INTRA-UTERINE INSERTION OF GRAFENBERG'S RING FOR CONTRACEPTION

H. H. MAYER

Chinese M. J., 66: 212-213, (April) 1948

The case of a 20-year-old Chinese housewife is presented. She was pregnant in spite of a metal ring inserted into the uterus by a doctor as a contraceptive device. As there was no sign of abortion or infection the patient was advised to carry the pregnancy to term in hopes that the ring would be expelled. The

so-called menopausal involutional melancholia, which is a definite psychosis of degenerative type not due to ovarian hormone withdrawal, and not curable by organotherapy, as some would have us believe. It is not to be confused with the mild degrees of mental depression which may occur at this epoch, and which all too frequently are due to the wrong ideas still held by many women concerning the supposed dangers of the menopause—the fear of insanity, the fear of cancer, the fear of losing physical attractiveness to the husband, the fear of becoming fat, etc. In the management of this rather large group, the sensible gynecologist can be his own psychiatrist, and he can thus accomplish far more with such patients than he can with organotherapy, which is only occasionally indicated, if there are associated vasomotor symptoms.

There are other simple psychiatric problems of this sort which can be handled by the gynecologist himself without calling in his psychiatrist confrere, especially as such a consultation still unfortunately carries with it what the patient considers a stigma, and may frighten her into thinking her mental problem is more serious than it is. On the other hand, the more serious problems, demanding expert and time-consuming social and psychiatric investigation, and sometimes involving such serious possibilities as suicide, should be handled only by the trained psychiatrist.

Much of the authors' discussion in the present paper deals with the difficult and sometimes insoluble problems of sex maladjustment. These often involve so many intimately personal or complexly social aspects that they receive very perfunctory and totally inadequate consideration from the busy practicing gynecologist, who should be only too glad to refer the more serious problems of this sort to the more intensive and more meticulous study of the psychiatrist. Contrary to a playful impression among their colleagues, not all psychiatrists are a bit "screwy" themselves.—Ed.)

GENITAL MALIGNANCY IN THE FEMALE

R. A. Ross

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South. Surgeon, 14: 651-658, (September) 1948

There has been moderate improvement in the mortality rates in genital malignancies since the first reports soon after the opening of Duke University Hospital in 1930. Multiple procedures are used to establish or rule out malignancy. A positive Frei or Wassermann does not rule out malignancy. Tissue from several areas removed for biopsy examination and curettements are the true criteria. The vaginal smear is used as a screening method.

The salvage rate is 33 per cent in 57 patients with cancer of the vulva. The preferred treatment is X-ray followed by radical vulvectomy and Bassett groin dissection. Recurrence was frequent and slow healing was the rule.

From 1944 to 1947, 530 patients with cancer of the cervix were treated. In 75 cases more radical surgery than the orthodox Wertheim operation was used and included hysterectomy, bilateral salpingo-oophorectomy, excision of a large part of the vagina, dissection of the ureter and ureteral obturator and the iliac nodes. Of the entire group, 51 were in clinical stage 1; there was inguinal node metastasis in 8 patients who did not have irradiation and in 3 who did. In stage

practise is a simple mastectomy through the smallest possible incision, followed by an intensive course of X-ray therapy. The estimated 5-year survival rate is 56 per cent of the operable group and 14 per cent of the inoperable group. These are considerably better than those reported by any other clinic.

Thus it seems necessary to re-evaluate the Halsted operation. The death rate from carcinoma of the breast is increasing. Prior to the publication of Halsted's paper in 1894, cancer of the breast was considered incurable. In 1907 Halsted reported 232 cases with a 38.3 per cent survival rate of 3 to 5 years.

In 1929 a report from 9 hospitals showed a survival free of recurrence for 5 years of 20 per cent of the group. Other survival rates published since are presented in the following table.

CLINICS	PERCENTAGE AXILLARY NODES INVOLVED AT OPERATION	PERCENTAGE 5 YR. SURVIVAL	
		Surgery alone	Surgery plus X-ray
Harrington.....	60	48.0	48.0
Lahey.....	62	38.6	52.0
Adair.....	65		53.0
Presbyterian Hospital.....	61	36.0	
St. Lukes Hospital.....	60	34.0	
Finney.....	45	49.0	
Ramsdell.....	60		42.0
		Simple mastectomy plus X-ray	
Edinburgh.....	80	56.0 (estimated)	

The author concludes from the statistics that there seems to have been a gradual improvement in the results reported since 1929. He feels that more time should elapse before accepting the 5-year percentages of the Edinburgh statistics, since they are based on cases treated from 1941 to 1945 and are estimated rather than actual figures. He feels that there is need to reduce the percentage of patients who wait until the disease has spread to the axillary nodes. He plans to continue with radical mastectomy and X-ray therapy.

(In cancer of the breast, as in cancer of the cervix, it is evident that the studies of the last 50 years have not yet permitted any unanimity of opinion among surgeons as to the best plans of treatment. As the author mentions, the most popular plan in this country has for many years been radical mastectomy with axillary gland dissection, although there has been less concordance as to the deep X-ray adjuvant. Formerly some used this only preoperatively, others postoperatively and some not at all. At present the postoperative use of X-rays appears to be the choice of most surgeons.)

The Edinburgh plan has excited great interest among American surgeons, but it has not achieved any wide adoption, in spite of the very comparable results reported, such as those of Ramsdell.—Ed.)

patient delivered a normal full term infant with a normal placenta but the ring was not found. A week after delivery an X-ray showed a dense ring shadow in the pelvic cavity. Dilatation and curettage did not reveal the ring. Some months later after another dilatation and curettage had been attempted by another physician, the patient was seen again complaining of sharp pain and vaginal bleeding. Perforation of the uterus made a supravaginal hysterectomy necessary. An X-ray later revealed that the ring was still in the pelvis, probably in the soft tissues behind the cervix.

Three other cases of uterine complications resulting from the use of the Grafenberg are presented. A small ring may be expelled by uterine contractions without being noticed and a large ring may erode into the soft tissues causing severe irritation, excessive discharge and even vaginal bleeding. Besides, it seems that the ring is not a dependable contraceptive device.

(I find it difficult to resist telling a ribald story in commenting on this case, the story of the bride-to-be who lisped, and who was showing her wedding presents to some of her girl friends. She showed the beautiful diamond "wrist-watch" from her father, a lovely "wing" from some one else, and so on. One of the friends asked, "But what did you get from John, your husband-to-be?" She blushing answered, "Oh, I can't show you that, because it's up in my woom." Morris Fishbein is welcome to this story for a more proper setting in his *Tonics and Sedatives*.

In the case described by Mayer the mystery of the missing ring is still unsolved, and it is apparently still reposing peacefully in the "soft tissues behind the cervix," in spite of the fact that the patient had a supravaginal hysterectomy, which will certainly be a better contraceptive than the ring proved to be. Nor is it clear from the above abstract at what stage of pregnancy the disappearance of the ring was noted, so the readers can be spared a learned and probably a very inconclusive discussion of whether or not a search party should have been organized earlier than it was.—Ed.)

CARCINOMA OF THE BREAST: A COMPARATIVE STATISTICAL STUDY

E. G. RAMSDELL

White Plains, New York

South. Surgeon, 14: 637-644, (September) 1948

There seems to be very general agreement in this country that the best treatment of carcinoma of the breast is radical mastectomy, consisting of the removal of pectoral muscles with a careful dissection of the axilla, followed, as soon as wound healing has been accomplished, by an intensive course of X-ray therapy. The 5-year survival rate averages from 40 to 50 per cent.

However, during the meeting of the International Surgical Society in September, 1947, a paper was presented by Dr. R. McWhirter reviewing the subject of carcinoma of the breast and its treatment by the Edinburgh group. The current

AUTHOR INDEX

JUNE, 1949

- Allen, W. M., 451
 Assali, N. S., 362, 396
 Atkinson, W. B., 424
 Austin, C. R., 441
 Ayre, J. E., 417
- Ball, T. L., 426
 Barns, H. H. F., 374
 Bartholomew, R. A., 349
 Beacham, D. W., 439
 Beacham, W. D., 439
 Beard, R., 380
 Benefield, M. L., 421
 Bernhard, P., 331
 Bowley, C. C., 372
 Brown, W. W., Jr., 315
 Brunschwig, A., 418, 420, 430
 Brust, A. A., 362
 Bryant, R. D., 396
 Burger, K., 373, 407, 432, 433
 Burns, E. L., 416
- Chalmers, J. A., 376
 Check, F., 447
 Cobb, S. W., 315
 Colvin, E. D., 349
- Diddle, A. W., 368
 Dubrauszký, V., 407
- Eastman, N. J., 399
- Farris, E. J., 450
 Ferris, E. B., 362
 Fish, J. S., 349
 Fouché, H. H., 377
 Fremont-Smith, M., 415
 Furuhjelm, M., 403, 404
- Goldman, D. W., 443
 Graham, R. M., 415
 Grant, A., 439
 Grimes, W. H., Jr., 349
 Gushberg, S. B., 424
 Gustafson, G. W., 387
- Habel, J. M., 404
 Haden, W. D., Jr., 422
 Haines, M., 328
- Haman, J. O., 441
 Hartl, H., 411
 Hershenson, B. B., 341
 Hingson, R. A., 350
 Hufford, C. E., 416
 Hunter, A. L., 422
- Ingelman-Sundberg, A., 428
 Irwin, J. K. L., 391
- Jacobi, H., 385
 Javert, C. T., 426
 Johnson, H. W., 359
 Joyce, J. B., 383
- Kaplan, I. I., 448
 Kerr, J. M. M., 333
 Kobrinski, S., 369
- Lennon, G. G., 383
 Long, R. V., 330
 Lull, C. B., 339
 Lynch, J. E., 394
- McCall, M. L., 363
 McDonough, J. J., 435
 McIntyre, J. P., 375
 Mackey, R., 439
 Maliphant, R. G., 423
 Mason, L. M., 410
 Mayer, H. H., 455
 Mayes, B. T., 393
 Mazer, C., 447
 Meigs, J. V., 415
 Mengert, W. F., 315, 335
 Mills, W. G., 366
 Mobray, R., 372
 Montgomery, T. L., 343
 Morgan, J., 382
 Morgans, M. E., 374
 Munnell, E. W., 420
 Murphy, D. P., 450
- Nixon, J. W., 425
- Paxson, N. F., 389
 Pedvis, S., 391
 Perry, S. P., 422
 Philpott, N. W., 391



Review

THE USE OF PITUITRIN BEFORE DELIVERY*

A REVIEW OF THE AMERICAN LITERATURE

NORMAN HERZIG,

New York, N. Y.

A reorientation by many obstetricians to the use of pituitrin before delivery is necessary. The improper use of the drug during the last four decades should not be the standard by which is measured its proper use today. Since the introduction of pituitary extract to obstetrics by Bell (1) in 1909, its use before delivery has been a controversial subject. Pituitrin, originally a trade-name, has persisted as the popular designation of the extract, and will be used throughout this report.

Most authorities maintain that pituitrin should not be given, except with caution, prior to the third stage of labor (2-4). Some permit it for the induction of labor, in limited dosage, but not in the management of the first stage. Many have found it useful for inertia appearing before full cervical dilatation; while others have confined the use of pituitrin to the treatment of second-stage inertia. There are few, today, who will recommend pituitrin for normal, uncomplicated labor.

This report, based on a review of the American literature, traces the development of the current attitudes on the use of pituitrin before delivery. The contributions of German, English, French and Latin American obstetricians, as well as others, have been as voluminous as those of our own writers. It became apparent, however, that once American obstetricians and general practitioners began to use pituitrin, they took their cue for its correct application from their American leaders.

Two self-imposed limitations in this report have been: (1) the elimination of consideration of other oxytocics like ergot, thymophysin, and methergine for the management of the first two stages of labor; and (2) the avoidance of discussion of the use of pituitrin in non-obstetric situations, in the treatment of abortions, and in the immediate postpartum period.

The American literature relating to the use of pituitrin before delivery may be divided into two parallel developments: (1) The immediate favorable acceptance of pituitrin which soon became a minority viewpoint that has persisted as such to the present; and (2) the unfavorable attitude to pituitrin which has been the predominant one since the early reports of accidents from the drug.

During the years before the discovery of the clinical effectiveness of pituitary extract in producing uterine contractions, the obstetrician used many drugs for the stimulation of the uterus when inertia occurred, usually without success (5).

* Read by invitation before the New York Academy of Medicine, Section of Obstetrics and Gynecology, March 22, 1949.

- Pierce, L. C., 408
Pollak, O. J., 449
- Ramsdell, E. G., 456
Reel, P. J., 427
Ridley, B., 452
Roberts, J. M., 346
Rommer, J. J., 443
Ross, R. A., 454
Roth, D. B., 445
- Seibels, R. E., 399, 414
Shenk, E. P., 343
Sigeler, S. L., 437
Simmons, F. A., 446
Simmons, J. M., 371
Simpson, K., 398
Snaith, L., 452
Spencer, J. A., 427
Stein, J. J., 406
- Steward, R. E., 343
Swenson, P. C., 337
Switzer, P. K., 377
- Taylor, A. G., 346
Taylor, E. S., 371
Thomson, G. R., 410
Turner, H. B., 350
- Underwood, F. J., 397
- Wallau, F., 379
Wells, S. M., 378
Welsh, A. L., 410
Whitacre, F. E., 350
Whitelaw, M. J., 438
Wichern, W. A., 425
Williams, M. F., 401
Williams, W. W., 440
Willson, J. R., 365
Wolff, W. A., 330

tions ascribed to it. Large doses used in the presence of malpresentation and disproportion would cause rupture of the uterus, he contended. Like Stein and Dover (57, 58), he felt that the principal virtue of pituitrin was its ability to make the uterus work efficiently in the first stage of labor.

The attitude of the majority of obstetricians was expressed by Kosmak (59) and by DeLee (60) at the meetings of the obstetrical section of the American Medical Association in June 1918. The former said that pituitrin had value if it were properly used; that is, "for a multipara, not exhausted, with secondary inertia during the second stage." The latter said, "I was one of the first to oppose the use of pituitary extract in labor. Laceration of the cervix is a complication the importance of which is being recognized more and more. It is nearly always caused if pituitary extract is used before the cervix is dilated."

Because of the misuse of pituitrin before delivery, many obstetricians accepted these opinions (61-69). The problem of what to do for the patient who required uterine stimulation during labor remained, nevertheless, and there were frequent attempts to solve it. Before considering these, the persistence of the idea that to use pituitrin before delivery was, as Eastman (70) recently stated he was brought up to believe, "the most heinous of obstetric sins," will be described.

DeLee, Kosmak, Adair, Williams, Davis and others emphasized the principle that to use pituitrin before delivery was dangerous for both mother and baby. Mendenhall (62) in 1921 quoted the statements of Edgar (14) and Polak (19) in 1913 on the dangers of pituitrin. Deutschmann (71) in 1925, citing Mundell (48) and Mendenhall (62), urged that the use of pituitrin in obstetrics be discontinued. Williams (72) noted that the standardization of pituitary extract was still non-existent in 1924, and quoted the work of McCloskey and Smith (73) who demonstrated in 1923 that different batches of extract used clinically varied as much as 8 times in potency.

During 1937, three important obstetric comments on pituitrin were published. Stander (74), who edited a symposium on obstetrics for the February 1937 issue of the American Journal of Surgery, stated in his introductory note: "As one reads these contributions, one is impressed with the conservative attitude of every author, although no attempt on my part was made to select or invite a particularly conservative group of obstetricians. This, then, must be evidence of the present trend in our field, as distinct from the time of accouchement forcé, manual dilatation of the cervix, universal prophylactic forceps, cesarean section on all patients suffering from eclampsia, and the use of pituitrin during the first and second stages of labor." Several of the authors, however, do recommend pituitrin in small doses for uterine inertia, abruptio placentae, and induction of labor (75-78).

The American Committee on Maternal Welfare published a Manual on Maternal Care, edited by Adair (79), in which it is stated that "the use of pituitary extract prior to delivery is dangerous." The only time its use was sanctioned by the Committee during the first two stages was in secondary inertia in doses of 1 to 2 minims when the patient was fully dilated, at home, no forceps available, labor stopped, and the vertex ready to be born.

The third general statement of importance in 1937 was that of Davis (80) who

Into this atmosphere of ineffectual therapy came the announcement by Bell (1) on November 4, 1909, that he had successfully used pituitary extract to stimulate the uterus in 5 cases. He suggested that pituitary extract "ought rarely to be given before delivery." On January 28, 1911, Hofbauer (6) reported his use of pituitrin as an oxytocic in 12 patients, and he noted that the pains "occur rhythmically and resemble normal labor pains."

The papers of Bell and Hofbauer revolutionized the treatment of uterine inertia (7-13). Druskin (7) commented, "Since the introduction of the antiseptic method in obstetrics by Semmelweiss and Oliver Wendell Holmes in the early forties, nothing has had such a far-reaching effect on the practice of midwifery as the use of pituitary extract." Humpstone (8), who reported in 1912 that his research showed "no discussion of the use of this drug before any representative obstetric body in this country," described 64 cases of inertia that received pituitrin in 4 c.c. doses with "brilliant results" in 18 patients. In a summary of the literature up to October, 1912, Lescohier and Closson (9) noted that pituitrin was uniformly recommended for uterine inertia of either the first or second stage, that it had been used with varying success for the induction of labor, and that the usual dose was 1 c.c. given hypodermically, repeated 3 to 4 times daily.

At the 1913 meeting of the American Gynecological Society, it was decided that the new drug, pituitrin, was very useful but dangerous (14-16). It could cause fetal asphyxia, lacerations of the cervix and perineum, placental separation and uterine rupture. It had its limitations and was to be used only in the second stage, cautiously. Dickinson (17) stated, "Where we are ready to anesthetize," pituitrin should be given. "It acts within 10 minutes and ceases in 30 minutes. The woman can thus throw in her last reserve. Strychnine will not do it. Opium is dangerous to the child. Pituitary extract has come to save the day."

From 1913 to 1916 the use of pituitrin was extended throughout the country. During these years, frequent reports of accidents and poor results appeared in the journals (18-47). Those who continued to emphasize its value in uterine inertia also pointed out the occurrence of uterine rupture. What made it difficult for the men using pituitrin was the fact that the drug was not standardized and that ampules of uneven potency were sold. Another factor was the use of large doses. One to 4 c.c. represented the average single injection.

Mundell (48, 49) summarized the data on the use of pituitrin in 1916 and 1917 with two collective reviews of the foreign and American literature totaling 3,952 cases and 1,293 cases respectively. He concluded that pituitrin was being improperly used in many instances, that its use should be limited to the multipara in the second stage of labor with secondary uterine inertia without disproportion, that it should not be used in normal labor, and he recommended that smaller doses be given so that "the dangers to the mother will be reduced to a minimum."

One of those who had reduced the danger from pituitrin was Bandler (50-56). He wrote many papers from 1914 to 1916 urging the use of $\frac{1}{2}$ c.c. doses. He argued that the drug should be given for the management of the first stage as well as the second stage; although it should not be given at all unless the obstetrician understood cephalopelvic relationships. Bandler was unique in his insistence that pituitrin could be used safely, without the occurrence of the many complica-

stetrics he exerted a strong influence on the obstetrical thought of his era. At first, he, too, praised pituitrin's value. Soon, however, as reports of poor results appeared, he reversed himself. He wrote repeatedly of the dangers of pituitrin, particularly of its causing uterine rupture. He did use it in $\frac{1}{2}$ minim to 3 minim doses for the induction of labor. The importance of DeLee's (107) influence can be demonstrated by this quotation from the 4th edition of his Text Book published in 1924. "Pituitary extract is being used extensively for weak pains both in the first and second stages of labor. It is a powerful oxytocic, increasing both contractions and tonus, and is one of the most dangerous medicines we have, doing untold damage to mother and child. Rupture of the uterus, lacerations of the cervix and perineum, death of the child from asphyxia and cerebral hemorrhage occur so often that the author cannot too strongly condemn its indiscriminate use." This paragraph appears unchanged in each subsequent edition including the 9th edition written by Greenhill (108) and published in 1947.

Two of the many objections to the use of pituitrin in labor have been that reactions and rupture of the uterus occur. Although the literature on rupture of the uterus has not been completely reviewed (109-115), pituitrin has usually been cited as an etiological factor in a small percentage of many reported series of uterine rupture. Yet it is usually concluded that pituitrin should not be used at all in labor, rather than that its use should be properly controlled.

The principal survey on rupture of the uterus due to pituitrin was written by Mendenhall (116) in 1929. He collected 89 cases, which he felt represented all the reported cases to that date. Of these, 62 were from the American literature. A personal check of the original articles from which this series was taken revealed that words like "injudicious" and "indiscriminate," which have appeared so often in the literature on pituitrin, were truly appropriate. Cases with full dilatation, cessation of labor, and questionable engagement of the presenting part were given 1 c.c. doses of pituitrin. Other cases of rupture, in which versions or forceps delivery through incompletely dilated cervixes were attempted, were ascribed to the use of pituitrin. While it is true that Greenhill (117) has cited a case of rupture of the uterus after the sixth 1 minim dose for induction, and that King (118) has described a case that received three 1 minim doses followed by a 2 minim dose with subsequent rupture, such reports have become rare in the literature of the past 9 years.

Sullivan and Heffernan (119) reviewed the literature on reactions to pituitrin in 1942. They commented, "It is evident from the reports in the literature and the wide clinical use of the drug that toxic side-effects occur in a very small percentage of cases." This review, like Sullivan and Heffernan's, has not disclosed the occurrence of one report of pituitrin sensitivity when doses of less than 3 minims were used. The majority of reactions were reported following the use of postpartum pituitrin in doses of one c.c. (120-124).

Among the investigative studies of pituitrin (125-140), the work of Murphy (133-137) has been outstanding. Using the Lorand tocograph, he has measured the amplitude, frequency, and character of uterine contractions before and during labor. He also recorded the effect of small doses of pituitrin on the parturient

said, "The oxytocic drugs are almost never indicated during the first and second stages of labor. It is dangerous to interfere with the normal uterine motility. Solution of posterior pituitary given during the course of labor initiates a marked tetany of the uterus."

These three pronouncements on pituitrin may be said to represent the logical reaction to the continued misuse of the drug. Four major contributions, however, made pituitrin less of an obstetric menace. The first was Watson's (81) introduction in 1920 of a method of induction of labor utilizing pituitrin; the second was Hofbauer and Hoerner's (82) use of intranasal pituitrin for both induction and stimulation of labor; the third was the standardization of pituitary extract, so that a unit-dose with a specific amount of drug could be used; and the fourth was the isolation of pitocin by Kamm (83) and his co-workers as a pure oxytocic fraction which could be used clinically without vasopressor effects.

Watson's method of induction was not immediately popular. Scott (84), his associate from Toronto, reported to the American Gynecological Society in 1926, that he had received 121 replies to a questionnaire he had sent to many members of the Society and to many Fellows of the American College of Surgeons. Forty-three men said they were using the method, while 78 said they were not. Scott concluded, "There is considerable confusion in the minds of many between the use of pituitary to induce labor, as opposed to its use during labor. It cannot be emphasized too strongly that when pituitary is used to induce labor, it should not be repeated once pains are established. To give the drug under such circumstances is the same as giving it early in the first stage of labor, and there is no question about such a procedure being fraught with danger."

The method of Hofbauer and Hoerner, which depended upon intranasal pituitrin, was more widely accepted at first by obstetricians. Reports describing the value of both techniques became frequent in the literature (87-97). The standardization and fractionation of pituitrin require no extended discussion (85). The facts themselves were sufficiently salutary to encourage further clinical experimentation with its use.

Another important development in obstetrics was the use of artificial rupture of the membranes for the elective induction of labor. Although many papers were principally concerned with artificial rupture of the membranes for induction, the use of 1 to 3 minims of pituitrin was frequently described. Rupture of the uterus attributable to pituitrin was not recorded in any of these reports (86-99).

The Committee on Induction of Labor reported to the May, 1939 meeting of the Central Association of Obstetricians and Gynecologists that among 125 anonymous replies to a questionnaire, there were 649 cases that were induced by a variety of methods with a 97.5% efficacy. A combination of quinine, pituitrin, and rupture of the membranes was described as the most popular (100). Thus, the trend towards the use of pituitrin before delivery continued concurrently with the trend away from that use.

To complete the picture of opposition to pituitrin, the effect of DeLee's attitude on the profession as a whole must be included (101-106). DeLee frequently discussed the use of pituitrin before delivery. As Editor of the Year Book of Ob-

be used in grand multiparity, where disproportion exists, or in doses larger than 1 minim.

During the discussion of this paper, Quigley (144) said, "About 1915 I read one of the earliest papers on the use of pituitary extract in obstetrics. Before 10 years had passed I began to regret the publication of that paper, which regret was prompted by several things. The first was the necessity of removing two badly ruptured uteri in a ward service and I have seen contraction-ring dystocia in some cases of my own. I cannot tell you how long ago I abandoned the use of pituitrin before the birth of the baby, but it must be at least 15 years. . . . Pituitary extract may be used with safety and I have no doubt that Dr. Eastman can use it with safety, but my point today is that I think it is bad teaching, a bad example to have go out from this organization. We have spent years in discouraging the use of pituitrin and we now rarely see it given, even by the general practitioner in our part of the country, and I am aware that after this paper we may encounter some ill effects that follow its use."

When Eastman closed the discussion, he said, "The question was brought up by Dr. Jacobs and several others as to whether we are doing the right thing in condoning in any way the use of pituitary extract, because it would be a bad teaching principle to go out from this Association. Dr. Quigley says that in Rochester the doctors are not using pituitary extract. That does not hold true in Maryland, and I have a feeling that general practitioners throughout the country, despite all the emphasis on the dangers of it, are employing it and in large doses, and I do not think we should be so naive as to think that any statement from this Association is going to have much effect on those men. They have tried it and achieved good results most of the time, and will continue with its use. It is my feeling that emphasis on contraindications and small dosage might do more good than the recommendation to eliminate its employment entirely."

In his editorial comment on these papers by Reid and Eastman, in the 1947 Year Book of Obstetrics and Gynecology, Greenhill (145) wrote, "It is not easy to discuss the two papers by Eastman and Reid. I well remember when pituitary extract was used extensively many years ago. I read of many disasters, heard of others not reported and witnessed a few." A further comment noted, "Results of the use of pituitary extract at Johns Hopkins and Harvard are excellent, but we must remember that these institutions are among the best in the world. It is therefore expected that the men on the staffs use pituitary extract judiciously, and when trouble arises they know how to overcome the difficulty with safety to mother and child."

The most recent development in the use of pituitrin before delivery has been the employment of the intravenous route of administration. In the literature described thus far, except for Hofbauer and Hoerner's intranasal pituitrin, the intermittent hypodermic method was always used. Although Hofbauer (146) suggested the use of intravenous pituitrin in doses of 2 minims per c.c. of saline in 1918 for induction of labor, the idea was not accepted. In 1943, Page (139) also reported the use of dilute pituitrin intravenously for uterine inertia with 10 or 20 units per liter of normal saline. Eastman (147) recently stated that the

uterus. His work has shown that the use of pituitrin can be placed on a more rational basis, and that such factors as uterine wall tension, the character of the individual uterus' response, and small doses of pituitrin are important. Rucker (64, 65) measured uterine contractility, too, and concluded that pituitrin frequently produced tetanic contractions of the uterus, and therefore, should not be used before delivery.

Other efforts to control pituitrin include the work of Dieckmann and Kharasch (138) who reported in 1942 the value of 'pitsulfonate', a slowly absorbing form of pituitrin; Page (139) who used pitocin tannate in oil in 1943 to prolong the oxytocic response without increasing the potency; and Abarbanel (140), who in 1945 studied the effectiveness of the magnesium ion as a spasmolytic in the pituitrin-induced tetanically contracted gravid uterus. Abarbanel found that the tetany could be prevented by the magnesium salts, provided they were given 3 to 5 minutes after the oxytocic.

These papers emphasized the virtue of pituitrin as an oxytocic provided small doses were used. Four reports in the past 9 years, which have focussed the attention of obstetricians on the modern use of pituitrin before delivery, are: Siddall and Harrel's (141) in 1940, Kassebohm and Schreiber's (142) in 1943, Reid's (143) in 1945 and Eastman's (70) in 1946.

Siddall and Harrel (141) reported the use of small doses of pituitrin in 62 cases of prolonged labor due to uterine inertia. Their results were good in two-thirds of the cases.

Kassebohm and Schreiber (142) reported 565 cases in which 1 and 2 minim doses of pituitrin were used routinely for the management of labor with the avowed purpose of reducing time consumption in labor because "The labor not completed in 18 hours bears the threats of hemorrhage, exhaustion and fetal mortality." The most important feature was the continuation of the drug until the second stage was reached. Two groups of patients, those induced and those whose labors began spontaneously, were treated in the same way. The virtue of the method was its avoidance of prolonged labor. Among the conclusions of Kassebohm and Schreiber was the fact that if prolonged labor were present when the patient was seen for the first time, the cautious use of pituitrin in small doses was indicated. There were no birth canal injuries, uterine ruptures, or maternal mortalities in this series.

In 1945, Reid (143) reported to the Boston Obstetrical Society a 5 year survey of 1609 cases of prolonged labor of 20 hours or more that received small doses of pituitrin. He noted that severe injuries to the birth canal and uterine rupture did not occur, that maternal mortality was not increased because of pituitrin, and that the incidence of prolonged labor was reduced.

Eastman's (70) report to the American Association of Obstetricians, Gynecologists, and Abdominal Surgeons in 1946 was concerned with the use of pituitrin in small doses in 463 cases. Among his conclusions, Eastman stated, "Having observed its ultra-cautious use in several hundred cases of uterine inertia, I am inclined to believe that the balance lies slightly in favor of pituitary extract—provided and provided again, that certain rigid rules be observed." It must not

be used in grand multiparity, where disproportion exists, or in doses larger than 1 minim.

During the discussion of this paper, Quigley (144) said, "About 1915 I read one of the earliest papers on the use of pituitary extract in obstetrics. Before 10 years had passed I began to regret the publication of that paper, which regret was prompted by several things. The first was the necessity of removing two badly ruptured uteri in a ward service and I have seen contraction-ring dystocia in some cases of my own. I cannot tell you how long ago I abandoned the use of pituitrin before the birth of the baby, but it must be at least 15 years. . . . Pituitary extract may be used with safety and I have no doubt that Dr. Eastman can use it with safety, but my point today is that I think it is bad teaching, a bad example to have go out from this organization. We have spent years in discouraging the use of pituitrin and we now rarely see it given, even by the general practitioner in our part of the country, and I am aware that after this paper we may encounter some ill effects that follow its use."

When Eastman closed the discussion, he said, "The question was brought up by Dr. Jacobs and several others as to whether we are doing the right thing in condoning in any way the use of pituitary extract, because it would be a bad teaching principle to go out from this Association. Dr. Quigley says that in Rochester the doctors are not using pituitary extract. That does not hold true in Maryland, and I have a feeling that general practitioners throughout the country, despite all the emphasis on the dangers of it, are employing it and in large doses, and I do not think we should be so naive as to think that any statement from this Association is going to have much effect on those men. They have tried it and achieved good results most of the time, and will continue with its use. It is my feeling that emphasis on contraindications and small dosage might do more good than the recommendation to eliminate its employment entirely."

In his editorial comment on these papers by Reid and Eastman, in the 1947 Year Book of Obstetrics and Gynecology, Greenhill (145) wrote, "It is not easy to discuss the two papers by Eastman and Reid. I well remember when pituitary extract was used extensively many years ago. I read of many disasters, heard of others not reported and witnessed a few." A further comment noted, "Results of the use of pituitary extract at Johns Hopkins and Harvard are excellent, but we must remember that these institutions are among the best in the world. It is therefore expected that the men on the staffs use pituitary extract judiciously, and when trouble arises they know how to overcome the difficulty with safety to mother and child."

The most recent development in the use of pituitrin before delivery has been the employment of the intravenous route of administration. In the literature described thus far, except for Hofbauer and Hoerner's intranasal pituitrin, the intermittent hypodermic method was always used. Although Hofbauer (146) suggested the use of intravenous pituitrin in doses of 2 minims per c.c. of saline in 1918 for induction of labor, the idea was not accepted. In 1943, Page (139) also reported the use of dilute pituitrin intravenously for uterine inertia with 10 or 20 units per liter of normal saline. Eastman (147) recently stated that the

group at Johns Hopkins had hit upon the idea of intravenous pituitrin in dilute solution about 1946, and that intramuscular administration had been "practically abandoned." Hellman (148) has reported in the past month an experience with 43 cases of uterine inertia treated with intravenous pituitrin. Finally, several similar unpublished studies (149) have been in progress in this city in recent months. The virtue of intravenous pituitrin in diluted dosage appears to lie in the easier control of the small amounts that are constantly supplied to the uterus.

DISCUSSION

In this review of the American literature on the use of pituitrin before delivery, it has been shown that the need for an efficient oxytocic in labor has always existed, and still does. Following the discovery of pituitrin, its early use with success was accompanied by much abuse with disastrous results. The reaction to the latter was profound, and soon, obstetricians limited the drug to the third stage where the reported accidents were few. Over the years, however, there were some who continued to depend on pituitrin because of its superiority to other uterine stimulants. The subsequent reduction in dosage, limitation of indications, standardization of the extract itself, separation of the oxytocic from the vaso-pressor fraction, and enunciation of contraindications have contributed immeasurably to our present knowledge of pituitrin.

One of the paradoxes in the application of this knowledge is the attitude of many obstetricians that pituitrin may be used for induction of labor, for the treatment of first-stage inertia, or abruptio placentae but that it must not be used for the routine management of the normal labor. A corollary to this idea is that once satisfactory uterine contractions have been obtained with pituitrin, the drug must no longer be given (150-154). Mathieu, Watson, DeLee, and Dieckmann, all of whom recommend the use of pituitrin as an effective aid to induction of labor, limit the total dosage which may be used. Page, Murphy and Abarbanel have pointed out the danger of repeated administration of pituitrin. Only Kassebohm and Schreiber have within recent years sanctioned the use of pituitrin throughout the first stage of labor. It is this idea which has been resisted so emphatically by most obstetricians, namely, that one can give small doses of pituitrin safely during the complete first stage, whether from the point of induction or after labor has begun spontaneously.

Another continuing attitude is the distrust of the use of pituitrin before delivery under any circumstances. It has been objected that although the use of pituitrin may be permissible for the expert obstetrician, it is not suitable for the general practitioner. Bartholomew (155) recently described the situation in many areas by saying, "Medical students and interns taught to shun pituitary extract during labor, do not maintain this attitude on entering practice. Observing the unrestricted use of pituitary extract by their fellow practitioners and impressed with its time-saving value, they use it freely, thereafter, with no regard for contraindications or dosage." It would seem to be the practitioner's responsibility to learn the correct use of pituitrin, if he is to use it, just as he does the proper dose of digitalis or morphine.

Whether pituitrin is used by practitioner or specialist is not so important as agreement about its indications before delivery. As Eastman commented, the emphasis must be on proper use and not prohibition.

CONCLUSIONS

The use of pituitrin before delivery as recorded in the American literature has been examined, discussed, and summarized.

Analysis of the development of current ideas about pituitrin has shown that a strong influence against its use before delivery has persisted since the early misuse of pituitrin.

The modern use of pituitrin has demonstrated that it can be a safe, efficient, and superior oxytocic before delivery.

Although one modern view sanctions the use of pituitrin in small doses before delivery with the limitation that the drug be stopped once uterine contractions have become regular, there has been evidence that pituitrin may be safely used continuously until delivery, and in this manner act as a prophylactic to the occurrence of uterine inertia or prolonged labor.

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Obstetrics

PHYSIOLOGY OF PREGNANCY, LABOR AND PUERPERIUM

PLASMA VOLUME AND EXTRAVASCULAR FLUID VOLUME DURING PREGNANCY AND THE PUERPERIUM

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Am. J. Obst. & Gynec., 57: 471-481, March, 1949

It was the purpose of this study to investigate the changes that occur during normal pregnancy in the circulating red-cell mass and plasma and extravascular fluid volumes, with the belief that determining the normal relationship between these three compartments in uncomplicated pregnancy might aid in evaluating changes occurring in abnormal pregnancy.

Six to 12 observations were made on each of 10 patients in this investigation. All were healthy multigravidae and primigravidae whose diets were adequate and nonrestricted and who were taking no medication during pregnancy or the puerperium. Observations were made at 5 to 6-week intervals; the earliest on one patient was made 230 days prior to delivery, and a determination was made on another patient in early labor. In the puerperium, volumes were determined at the end of the first week in 5 cases, and the last postpartum observations were made on the 26th to 66th days of the puerperium. Plasma volume was measured by using the blue dye T-1824 by the technique of Gibson and Evans. Extracellular fluid was measured by the use of intravenous 5 per cent sodium thiocyanate. Thiocyanate was determined using the method described by Chesley. Since the plasma volume is included in the thiocyanate space, extravascular volume could be calculated. Patients were admitted to the hospital the morning preceding the test, and after a fat-free lunch, an injection of 5 per cent sodium thiocyanate was given intravenously. All urine voided during the next 18 to 20 hours was collected. The next morning, under fasting, basal conditions, 10 mg. of T-1824 and 100 cc. of whole fresh radioactive blood were given to measure simultaneously plasma volume and the circulating red-cell mass. A serum sample for thiocyanate concentration was taken prior to this injection. Heparinized samples of whole blood were then withdrawn without stasis at 10-minute intervals for 50 minutes.

Without exception, there was a progressive increase in plasma volume up to approximately 68 to 5 days prior to the onset of labor. This increase averaged 1,366 cc. In 8 full-term pregnancies, there was an average prelabor decrease of the plasma volume of 347 cc. from its mean maximum value. In the other 2 cases the prelabor values remained stationary; one was a full-term mild pre-eclamptic

pregnancy and the other a case of premature labor. The plasma volume increase during pregnancy was 49 per cent when compared with nonpregnant values 30 days after delivery. The prelabor decrease of plasma volume averaged 25 per cent of the total increase which had occurred during pregnancy. Plasma volume had returned to normal nonpregnant values by the 30th day after delivery.

There was an increase in the amount of extravascular fluid up to the onset of labor. The rate of increase was accelerated during the last trimester with no evidence of any prelabor decrease. The average total increase in extravascular fluid volume during the period of pregnancy studied was 4,600 cc. With the exception of one case, the peak volume was reached during the 11 days preceding the onset of labor. At the end of the first week of the puerperium, an average decrease of 2,500 cc. had occurred. The extravascular fluid volume, when measured for the final time between the 26th and 66th days of the puerperium, was 59 per cent below the maximum prepartum value.

The vascular and extravascular spaces, which make up the extracellular fluid compartment, retain fluid at different rates and amounts in each trimester of pregnancy. A significant change in the ratio of the absolute changes in extravascular fluid to plasma volume is first noted approximately 160 days prior to the onset of labor. Although the volumes of plasma and extravascular fluid are each increasing during early pregnancy, plasma volume is increasing to a much greater degree than extravascular fluid. This ratio continues through the second and into the first part of the last trimester. Approximately 80 days prior to the onset of labor, there is a marked reversal of the ratio. This change is the result of an accelerated increase in extravascular fluid volume which is further augmented by the decrease in plasma volume occurring about the 40th day prior to delivery. At delivery and in the puerperium when checked at 7 and 30 days, there is no significant difference in the ratio. 6 figures.

(Such an abundance of valuable data is presented in this paper that it was feasible to abstract but a portion of them. One extremely important observation made by the authors, not described in the above digest, is mentioned almost parenthetically in their section on "Material and Methods." In order to answer a criticism that the dye which they used for determining plasma volume might be trapped at the placental site and hence might not be thoroughly mixed, the following procedure was carried out. A patient with a normal term pregnancy while under spinal anesthesia and prepared for an elective cesarean section, was given 10 mg. of T-1824 and 50 cc. of whole fresh radioactive red blood cells in the left antecubital vein. Prior to this injection, the left uterine vein had been cannulated with polyethylene tubing. The tip of this tubing was placed as far into the uterus as possible. Simultaneous samples of heparinized whole blood were then withdrawn from the cannulated uterine vein and from the right antecubital vein at 1, 3, 5 and 7 minutes after the injection of the blood and dye. When the plasma samples were checked photocolometrically, the dye concentration in the uterine and arm samples was the same. No difference was found in the radioactivity of the blood samples which were withdrawn simultaneously. The authors regarded this as evidence that the blood is not trapped at the placental site during its circulation through the uterus in a full term normal pregnancy.

Although this is only one observation, it represents a step toward ascertaining the rate of blood flow in the uterus. Information on this question is much to be desired from a number of viewpoints. Thus, it is prerequisite to any thorough documentation of the uterine ischemia theory of eclampsia. It is also tied up with the problem of placental transmission. It has

long been maintained, on the basis of evidence which I cannot trace down, that blood flow through the intervillous spaces is sluggish. At variance with this old concept of a sluggish placental circulation, are the studies of Flexner, Vosburgh and their associates, which show that water and other substances pass back and forth across the placental barrier at an unbelievably rapid rate. Likewise contradicting it are the findings in the above experiment which indicate that within one minute substances injected into an arm vein are thoroughly mixed in the venous blood of the uterus. This, of course, is only a beginning, but it is to be hoped that in the next few years further observations on uterine blood flow in pregnancy will be forthcoming.

The investigation of extracellular fluid volume in pregnancy has been fraught with sundry difficulties. One of these is that the thiocyanate space—the body spaces throughout which the test substance, thiocyanate, diffuses and the extent of which is equivalent to the amount of extracellular fluid present—includes that theoretical portion of the intravascular space which is filled with plasma water. Since plasma volume increases greatly in pregnancy, as this and other studies show, this large mass of changing intravascular fluid must be given due consideration. The present authors have taken care of this most satisfactorily by performing separate plasma volume studies so that their figures are for extravascular, extracellular fluid volumes only. More difficult to evaluate is the extracellular fluid volume of the fetus, amniotic fluid and the enlarged uterus. Only when this is established, can one be at all certain about alterations in actual maternal tissue hydration in pregnancy. The above authors and also Chesley (*Surg., Gynec. & Obst.* 76: 589, 1943; *ibid* 77: 261, 1943) have given this source of error careful consideration and have allowed for it in their calculations. The upshot of it all seems to be something as follows. During the first 30 to 34 weeks of pregnancy the increase in extracellular, extravascular fluid volume is attributable entirely to the increase of the thiocyanate space created by the growing fetus, the amniotic fluid and the uterus. But at about that time a change occurs in the bodily economy of such a nature that some 8 or 9 pounds of water become gradually added to the maternal tissues in the form of extracellular, extravascular, extra-uterine fluid.

Just what causes this change in water balance in the latter part of normal pregnancy? Of course, no one knows. It will be noted, however, that the time when it occurs is also the period when preeclampsia and eclampsia begin to appear. This observation serves to recall that the toxemias of pregnancy, in all probability, are simply physiologic processes gone awry; it serves also to emphasize how important such fundamental studies as the above will doubtless loom in the eventual elucidation of those complications.—Ed.)

CHARACTERISTIC CHANGES IN THE FETAL HEART TONES

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Zeitschr. f. Geburtsh. u. Gynäk. 124: 274, 1942

The author describes 4 different types of fetal heart tone curves which may be considered abnormal. They are as follows: (1) a rise of the heart rate above 160; (2) a drop in cardiac rate below 100; (3) a variation in rate of at least 40 beats per minute; and (4) a sudden drop to below 100 after an initial rise to 160. For the purpose of this study fetal cardiac arrhythmias are omitted.

The author studied 2370 deliveries occurring in his clinic during the 2-year

period from February 1, 1937 to February 1, 1939. Of these deliveries, 540 (22.8 per cent) showed abnormal heart tones. Four possibilities for the causation of these abnormalities are postulated. (1) The cardiac rate is altered as the result of delayed rupture of the membranes. It improves immediately after spontaneous or artificial rupture of the membranes. This is called "delay effect." (2) The fetal cardiac rate is altered after spontaneous or artificial rupture of the membranes. This is called "membrane-rupture effect." (3) "Entry effect." The cardiac rate is altered as the head enters a narrow pelvis. (4) "Exit effect." The cardiac rate is altered as the head comes out of the pelvis and passes through the soft parts.

In 540 cases, delay effect was observed in 10, membrane-rupture effect in 17, entry effect in 13 and exit effect in 148. Of the remaining 352 cases, 182 were due to such intercurrent causes as transverse presentation, toxemia and tumultuous labor; 119 curves could not be definitely explained; 22 cases were excluded because of an insufficient period of observation, and in 29 cases in which the curve did not fall into the above mentioned 4 groups, the baby died in utero.

In the remaining 188 cases detailed studies are as follows: *Group 1, Delay Effect.* This effect was observed 10 times in 188 cases. In 6 cases the fetal heart tones showed a rapid fall and in 4 cases a rapid or gradual rise. All fetal hearts improved following rupture of the membranes. There was no mortality. Various authors have explained this effect by stating that there is an increased amniotic fluid pressure or increased force of uterine contraction because of the resistant membranes, producing in turn pressure upon the head and a vagal effect upon the heart. There is no indication for forceps or rapid delivery in this group as all the infants improve after rupture of the membranes.

Group 2, Effect of the Rupture of the Membranes. This effect was observed in 17 cases, in 2 of which the fetal heart tones rose above 160, in 11 of which it fell below 100 and in 4 of which it varied more than 40 beats per minute. In 9 of the cases the fetal heart tones remained abnormal until delivery. Only one case was severely asphyxiated at delivery and all infants survived. The effect of rupture of the membranes occurred principally when the latter was artificial and was probably due to a sudden change of pressure upon the fetal skull. It does not constitute an indication to rapid delivery.

Group 3, The Entry Effect. This effect was observed in 13 cases, in which there were no deaths. The heart rate deteriorated with entry of the head into a contracted pelvis. Of the 13 cases, 8 were perfectly normal at delivery and in the remaining 5, in which 3 were delivered by forceps, there was slight asphyxiation. In general, conservative treatment is best here also. The effect is not maximal at the time of greatest pressure upon the skull but immediately after the resistance of the narrow pelvis has been overcome. It is believed that it is a sort of "negative commotio cerebri."

Group 4, The Exit Effect. In this group the fetal heart rate deteriorates upon exit of the head through the pelvis and passage through the soft parts. There were 148 such cases, in 65 of which there were umbilical cord anomalies; that is to say, in 18 of these cases the cord was less than 45 cm. long, in 21 it was loosely wrapped around the body and in 26 cases it was tightly wrapped around the body. In these

148 cases there were 3 deaths of which 2 had cord anomalies; 35 of the babies were slightly asphyxiated and 10 were badly asphyxiated. It is plain that this group is much more significant than the other 3. In the group without umbilical cord anomalies 9 fetal hearts rose above 160 beats per minute, 56 fell below 100 beats per minute, 3 varied more than 40 beats per minute and 15 rose above 160 and then suddenly fell below 100 per minute. The one death in this group occurred in a child whose fetal heart rose above 160 and then suddenly sank below 100.

Of the 83 patients in the group without umbilical cord anomalies, 64 were primigravidae.

The author feels that resistance of the fetal soft parts, with pressure upon the head, is a significant cause of fetal heart rate anomalies in this group. Other possibilities include a rise of blood pressure in the fetal circulation, if fetal blood is pushed out of the placenta by violent uterine contractions; by lack of oxygen as a result of slow premature separation of the placenta immediately preceding delivery; and finally, because of wrapping of the cord around the infant with resulting compromising of the infant's blood supply.

The danger in the last group, the exit effect group, is so great that a rise of heart tones above 160 beats per minute is viewed by the author as an indication for rapid termination of labor.

(Owing to the war and its aftermath, it is understandable that the German literature is still somewhat meager. Moreover, the foreign journals have been very slow in coming through, as the above date would indicate. All this is doubtless a temporary circumstance, but meanwhile it is the desire of the Editors of the Survey to bring to its readers occasional articles of European origin. At the present juncture, the yield may not be so good but as time goes on it is hoped that the thoroughness and originality of thought which long distinguished the German obstetrical and gynecological literature will enjoy rebirth and that we shall be justified in devoting a larger number of pages to contributions from that and other European sources.

The above article is included because it deals with an extremely practical and fundamental topic, but one which has not received the intensive study it deserves. However, most obstetricians, I imagine, would disagree with several of the contentions set forth. Thus, the statement that excessive pressure by the amniotic fluid may occasionally cause slowing of the fetal heart is open to question and is certainly at variance with my own experience; in addition, it is a dangerous teaching to promulgate. Equally untrue, and much more dangerous is the teaching that a heart rate of 160 late in labor (the exit group) is an indication for immediate delivery. The fallacious notion that a very rapid fetal heart rate is a sign of fetal distress has been a hard one to down;—so much so that although most obstetricians realize it isn't true, they nevertheless worry about the baby under such circumstances. The evidence against this viewpoint is rather overwhelming. One of the first to contribute such evidence was Bartholomew who pointed out in 1925 that rapid fetal heart rates were not serious and, moreover, were infrequently heard (*Am. J. Obst. & Gynec.* 10: 89, 1925). Sontag reported an incidence of fetal tachycardia of 72 to 76 per cent during the last 2 months of pregnancy (*ibid* 40: 449, 1940). Lund's careful study of fetal heart rates by means of a special recording device, the Endocardiograph, provided no evidence that tachycardia indicates fetal distress. In his opinion, tachycardia most often results simply from fetal activity (*Ibid* 45: 636, 1945).

The frequency with which the fetal heart slows at some time or another during labor (between contractions) without demonstrable cause or significance, as pointed out by the author, is well worth noting and is in keeping with common experience. As Lund has empha-

sized, if studies of this kind are to be undertaken, they should be done with some recording device since simple audition and timing with a stopwatch is well nigh worthless for research purposes.—Ed.)

MEASUREMENT OF THE RATE OF VENOUS BLOOD-FLOW IN THE LEGS OF WOMEN AT TERM AND IN THE PUERPERIUM, USING RADIOACTIVE SODIUM²⁴

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J. Obst. & Gynaec. Brit. Emp., 56: 36-40, February, 1949

Foot-groin venous blood-flow estimations have been made in 50 obstetrical patients, using radioactive sodium, Na²⁴. These women were examined during the first stage of labor and again between the fourth and tenth day of the puerperium. The group included 39 primigravidas; the rest had already borne one to 5 children. Cases of severe varicose veins were not included in the study.

Prior to examination, the patient's leg was immersed in a 40 degree C. water bath for 10 minutes to insure vasodilation. One ml. sterile saline containing 5-10 microcuries of radioactive sodium was injected rapidly into a vein in the dorsum of the foot, and the arrival of the radioactive material in the femoral vein at the groin was recorded electrically on a kymograph. Average rate of blood-flow could then be calculated from the time between injection and arrival of the Na²⁴Cl at the groin and the length of the patient's leg.

The results obtained have been compared with those in a control group of 50 normal nonpregnant women. In the first stage of labor, the range of flow-times was much increased, while the mean for the group fell at the extreme upper limit found in normal subjects; the foot-groin times fell outside the upper normal limit in 18 cases. The return to normal rate of flow during the puerperium was striking; within the first 10 days the range of flow-times diminished and the mean for the group was almost identical with that of normal subjects. In 11 women who were confined to bed during the puerperium, a similar return to normal was noticed. This suggests that the decrease of pelvic pressure after delivery has, in these cases, a greater influence upon the rate of blood-flow in the legs than has confinement to bed for a few days. These women, moreover, though not allowed to walk, received active exercise and massage.

The authors speculate on whether those patients who undergo venous thrombosis in the postpartum period either fail to regain a normal venous flow-time or have an abnormally rapid cytological and chemical response to the trauma of parturition, so that, in them, all the conditions (tissue damage, blood change and venous stagnation) favoring the onset of venous thrombosis are present together. 2 figures.

(Here is another important fundamental study based on the employment of radioactive isotopes. In brief, the authors find that the time required for labeled sodium chloride to ascend a leg vein is greater at term than in the nonpregnant. This is in agreement with McLennan's work on femoral venous pressure in pregnancy (*Am. J. Obst. & Gynec.* 45: 568, 1943) and also in keeping with the age-old clinical impression that a certain degree of venous stagnation occurs in the leg veins during late pregnancy. Although various theories have been advanced to explain this state of affairs, such as the placental arteriovenous shunt mechanism of Burwell, it would appear that the simplest explanation is the correct one, namely, the obvious obstruction to return blood flow offered by the enlarged uterus. Thus, McLennan has found that patients with large pelvic tumors exhibit elevations of femoral venous pressure entirely comparable to those seen in late pregnancy. These pressures return to normal values after removal of the tumor masses. He has likewise found in the course of cesarean section that femoral venous pressures usually show a marked decline after the removal of the fetus.

All this work on femoral venous pressure and flow time would indicate that within a few minutes after delivery, the dynamics of the femoral circulation have returned to normal and that venous stagnation of the femoral system is not a normal accompaniment of the puerperium. The main factors responsible for venous thrombosis in the puerperium must therefore be otherwise,—namely, the old offenders, trauma and infection, plus the very high blood fibrinogen levels which are so characteristic of the puerperium.—Ed.)

MANAGEMENT OF NORMAL PREGNANCY, LABOR AND PUERPERIUM

SIMPLIFIED METHOD OF FETAL ROENTGENCEPHALOMETRY: RESULTS CHECKED IN 482 CASES

R. TORPIN AND J. L. ALLGOOD

University of Georgia, School of Medicine, Augusta, Georgia

Am. J. Obst. & Gynec., 57: 455-460, March, 1949

At the present time, there are several methods of x-ray pelvimetry that quickly reveal the exact size and contour of the pelvic cavity. The ideal is to have such knowledge of the pelvis of every obstetric patient. However, unless one knows the size of the crucial diameters of the fetal head in question, the mechanics of obstetrics is still largely guesswork, as it has been in the past.

Because of the growing popularity of the lateral soft tissue technique in determining the condition of the fetus and placenta, it would be desirable, in addition, to obtain measurement of the fetal head. The writers have employed the isometric method, consisting of a single addition to the commonly employed lateral soft tissue technique, in a series of 482 cases. Their results are presented in this paper.

It is pointed out that the concept of the fetal head must be clearly defined. Briefly, the head is essentially cylindrical, one end of the cylinder being the face and the opposite end the occiput with the greatest circumference embracing the biparietal and suboccipitobregmatic diameters. Since in almost all cases the fetal head goes through the pelvic cavity with one end of the cylinder presenting, it is necessary to know only the diameter of the cylinder and this is obtainable by ascertaining either the biparietal or the suboccipitobregmatic diameter, since they are, or can be made by molding, essentially identical. A review of a large number of term newborn heads measured soon after birth demonstrated that they tend to range mainly from 8 to 10½ cm. in diameter, biparietal or suboccipitobregmatic. These two diameters seldom vary more than one centimeter from one another and the variation is almost always due to head molding in labor or to lack of it.

The addition to the lateral soft tissue technique employed in this study is that of attaching over the fetal head and as near it as possible a 10 cm. lead scale strapped over the mother's abdomen. It is necessary that this scale lie in a longitudinal plane on an elevation as near the center of the fetal head as possible. When the film is exposed, the scale image may then be used to measure by calipers the diameter of the fetal head in the plane of the biparietal or suboccipitobregmatic diameter, whichever is obtainable. This study revealed that where due care was taken in placing the marking scale at the level of the fetal head and correct placement of the patient, the error may be kept at 5 per cent plus or minus, i.e., 0.5 cm. It is pointed out that the object is for practical aid in prognosticating the course of labor and that the method cannot compete with more exacting, but more cumbersome and more costly triangulation methods. A test of its practical

value has been that, during the 7 years of its routine employment in all doubtful labors, the operative delivery incidence has been reduced to approximately one per cent, including forceps and cesarean section. Ninety-nine per cent have delivered vaginally, spontaneously, the only aid having been episiotomy and, rarely, Kristeller expression.

In the present series of 482 cases, in 321, or 66.7 per cent, the x-ray measurement was within 0.5 cm. of the actual size of the fetal head. In 427 cases, or 88.7 per cent, the x-ray measurement was within 1 cm. of the true size of the fetal head. In all cases with an error of more than 1 cm., the error occurred in taking the x-ray exposure, the marker being placed by inexperienced personnel. 3 figures.

(Both clinical and x-ray methods of estimating fetal size are notoriously unreliable and Torpin and Allgood's study, which constitutes an attempt to work out a more satisfactory roentgen technique for this purpose, is hence most welcome. It should be noted, however, that even with the refinements described the precision of the procedure is decidedly less than that of x-ray pelvimetry, with an error of plus or minus 0.5 cm. This means that if a given case shows a biparietal measurement with this method of 9.2 cm., the actual dimension is somewhere between 8.7 and 9.7 cm. The former figure indicates a relatively small head and the latter a rather large one. From Figure 3 of the original article it can be calculated, moreover, that the error is 0.3 cm. or less in only about 42 per cent of the cases, whereas in the remainder it is greater than this with considerable spread. These remarks are not made to discredit the method but rather to show that even in an expert's hands, such as Torpin, roentgen cephalometry still leaves much to be desired.

The operative incidence reported by the authors, namely 1 per cent including both forceps and cesarean sections, is the lowest of which I have ever heard. Of their patients "Ninety-nine per cent have delivered vaginally, spontaneously, the only aid having been episiotomy and, rarely, Kristeller expression." When I think of the incidence of cesarean section in my own clinic of about 5 per cent, of indicated forceps of 10 per cent plus a higher frequency of elective forceps, this figure of 1 per cent leaves me in a state of bewilderment. I have obtained some comfort, however, from the fact that the operative statistics of most other clinics, rightly or wrongly, are nearer to ours than to those at the University of Georgia. In Torpin's book, "Obstetric Labor," which by the way, is a goldmine of obstetric information (Augusta Obstetrical and Gynecological Book Company, Augusta, Georgia), he states that their operative incidence at the time of his writing was less than 3 per cent, about $2\frac{1}{2}$ per cent forceps and $\frac{1}{2}$ of 1 per cent cesarean sections. Torpin and Allgood imply that the further reduction to 1 per cent is attributable in part at least to the method described. This may be true, but this extremely low operative incidence means first and foremost a basic philosophy of obstetrics which is different from that which obtains in most other clinics. Whether, by reason of this 1 per cent figure, it is necessarily a better philosophy, I am not so sure.—Ed.)

PAIN IN CHILDBIRTH: STATISTICAL ANALYSIS OF SOME REPLIES TO THE QUESTIONNAIRES

K. K. CONRAD

Brit. M. J., 1: 333-339, February 26, 1949

The Subcommittee on Pain in Childbirth was set up by the Council of the Medical Women's Federation to obtain information regarding relief of pain in

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are likely to be more apprehensive and tense than the average parturient and hence need Grantly Read training rather than drugs. Perhaps, like most women, they need both types of therapy.—Ed.)

INTRAVENOUS DEMEROL-SCOPOLAMINE AMNESIA DURING LABOR

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Anesthesiology 1: 10, 1949

The authors present 100 cases in which demerol hydrochloride and scopolamine hydrobromide were given intravenously during parturition. The onset of true labor in any normal primipara or multipara was the only indication necessary for the first administration of the demerol and scopolamine. One cubic centimeter of the solution contained 10 mg. of demerol hydrochloride and 0.064 mg. of scopolamine hydrobromide.

The solution was given slowly until sedation seemed adequate. The initial dosage for patients who had received no previous drugs was usually 8 to 10 cc., and the initial dosage for patients who had previously received central nervous system depressant drugs was 5 to 7 cc. The second intravenous injection was required from 2 to 4 hours after the initial administration—the dosage was usually 3 to 5 cc. The dosage for the third injection was 2 to 4 cc.

Six patients (6.5%) required a 4th injection and 2 patients (2.1%) required a fifth injection. The average dosage for both groups of patients for the 4th and 5th injections was 1.5 cc. of solution. It was apparent that the interval between the need for additional amounts grew longer with each injection, and that the amount of drugs necessary to produce the desired effect each time was roughly one-half that of the preceding dosage.

Of the 100 cases studied, 59 were primiparae and 41 were multiparae. Both white and colored patients were observed, with ages ranging from 14 to 39 years.

No appreciable alteration of the course of the first stage of labor was noted; the second stage was characterized by hard, prolonged uterine contractions with adequate relaxation and rest between each pain. A significant observation was that the patients, as a whole, were not as irrational as those who had received other forms of amnesia during labor.

The incidence of apnea neonatorum was low. The previous or simultaneous administration of barbiturates or morphine with demerol resulted in a greater incidence of apnea of the newborn. It was necessary to reduce the amount of demerol administered under such circumstances.

The degree of amnesia was recorded from subjective examination. Amnesia was found to be satisfactory in 85.9% of the patients and unsatisfactory in 14.1%.

childbirth from married women doctors with children of their own. A questionnaire was sent to about 300 medical women, and 196 replies were received from those whose youngest child was not over 10 years of age. Analysis of the replies shows that *women doctors who themselves have had children are almost unanimously in favor of relief of pain in childbirth*. To the question: "Do you consider that relief of pain in childbirth is necessary?", 178 replied in the affirmative.

Analysis of the method of delivery showed a high incidence of forceps delivery in primigravidae. No adequate explanation can be given for this.

Analysis by place of confinement and by professional attendant showed that the majority of medical women are confined in private wards of hospitals and nursing-homes and the majority are cared for by obstetric specialists.

Analysis of anesthetics given mainly in the second stage of labor showed that *this group of women found chloroform by far the most efficient anesthetic agent*. Most of these births took place before trilene came into wide use in obstetrics. The efficacy of gas-and-air and gas-and-oxygen appeared to be enhanced by the presence of a trained anesthetist.

The small size of the sample precludes any definite opinion on the relative efficacy of the various drugs and sedatives given in the first stage of labor. However, the results showed considerable dissatisfaction with potassium bromide and chloral mixtures.

Out of a total of 409 deliveries for which these women answered the question: "Were you left alone longer than you liked?", 65 answered in the affirmative. Few mothers were made to walk about during their labors when they would have preferred to lie down.

A rather large proportion of the mothers stated that they would have liked more complete relief, 123 out of 425 deliveries, or 29 per cent for the first stage, and 103 out of 425 deliveries, or 24 per cent for the second stage.

Of the 196 mothers, 131 found that the memory of pain in childbirth faded quickly.

The situation with regard to anesthetization for perineal repairs was as a whole satisfactory.

No information of practical use regarding the value of antenatal exercises or of preparation for childbirth could be obtained, although two questions on these points were asked.

The subcommittee feels that this investigation has yielded some important information and also indicated possible lines of future investigation into the conduct of childbirth. Medical mothers represent a specially privileged group, and the type of care that they receive cannot, at least for many years, be made available to all mothers. It is hoped that it will not be long before adequate means of pain relief are made available to all mothers.

(This is an interesting and unique report because all the patients were women physicians and presumably in a position to evaluate intelligently their experiences in labor. But like many other investigations based on questionnaires, it lends itself to various interpretations. On the one hand, it may be taken on its face value to mean that these women should have had more sedative drugs in labor or perhaps caudal. On the other hand, it can be maintained that women physicians, because of their own professional training, reading and experience,

Of the total group, those showing absent hiatus appear to represent the basic minimum of failure, or 7.7 per cent. Hingson and Edwards, who have probably performed more caudal blocks than most anesthetists, report 8.8 per cent failure and 12.2 per cent partial failure. In the light of the present study, this approaches very near to perfection. It would appear that anatomic knowledge, skill and experience play a large part in decreasing the percentage of failures.

Caudal block is a highly useful technique with a wide margin of safety, and in the hands of an experienced anesthetist it is a relatively simple procedure. The writer suggests that in those cases in which caudal anesthesia is essential for patient safety, x-ray studies of the sacrum will provide a valuable means of combating failure, as in many cases anesthesia may be possible but difficult due to structural changes and defects. 5 figures.

EARLY AMBULATION IN OBSTETRICS AND GYNECOLOGY

S. PILLSBURY

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California Med., 70: 202-204, March, 1949

The author has found early ambulation to be a large factor not only in decreasing many of the complications that may follow childbirth and gynecological operations, but in reducing the time of convalescence.

Early in 1946, early ambulation was instituted at Seaside Memorial Hospital in Long Beach. As an increasing percentage of patients were permitted early ambulation, there was a concurrent decline in maternal morbidity from 3.7 per cent in 1946 to 2 per cent in 1947. During this period there were 4,178 deliveries, including cesarean sections, without a maternal mortality. While no doubt there were other factors contributing to these low figures, early ambulation must be given its share of the credit. Only one case of thrombosis occurred during this period, and it was in a patient who did not get out of bed until the fifth day.

The routine at this hospital is to have the patient dangle her feet over the edge of the bed several times a day 12 hours after delivery, and to have her walk around the room several times after 24 hours. She is permitted to walk down the hall and to have bathroom privileges after 48 hours. She is also encouraged to move about in bed as much as possible at all times. The maximal time for remaining in bed has been set as 24 hours because it has been shown that thrombosis of the extremities usually occurs within 2 to 4 days following tissue injury and stagnation of circulation.

By early use of the muscles, circulation is increased, thereby accelerating healing and a return to normal of all body functions. It is felt that the increased circulation is a great factor in early involution of the uterus, and that the upright posture gives better drainage of lochia. Early rising encourages deeper breathing

The analgesic properties of demerol were found to be excellent (no evidence of pain) in 2.2%, good (marked relief from pain) in 44.5%, fair (some relief from pain) in 33.7%, and poor (no appreciable relief from pain) in 19.6% of the patients.

(Demerol is so widely and satisfactorily employed throughout the country for obstetric analgesia, that its relative safety and efficacy when used judiciously, cannot be very seriously questioned. Certain precautions must be kept in mind, however, especially when it is administered intravenously. In the first place, as emphasized by Schumann, the period of injection must be very slow and extended over a full 2 minutes (*Am. J. Obst. & Gynec.* 47: 93, 1944). Otherwise, the patient invariably vomits immediately, and very shortly her pulse becomes rapid, irregular and thready, with a gradual return to normal (Schumann). In the second place, there seems to be a harmful synergistic action on the baby when demerol is combined either with morphine or the barbiturates, as noted by the above authors, and such combinations should be avoided. My own experience with demerol has not been quite so happy in respect to the baby as that generally reported, and it would be my feeling that the intravenous dose, even when given slowly, should be limited to 50 mg.—Ed.)

ANATOMIC REASONS FOR CAUDAL ANESTHESIA FAILURE

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Current Researches in Anesth. & Analg., 28: 33-39, (Jan.-Feb.) 1949

There will always be a small group of patients who are excluded from caudal anesthesia by reasons of infection, deformity, physical or emotional status, and the physician who is untrained in technique provides a further source of failure. With all these factors taken into account, there is still an average additional 20 per cent in whom we fail to achieve entirely satisfactory anesthesia and for which on the surface there is no adequate reason.

A total of 104 sacra were examined and measured by the author. These sacra showed abnormalities which would influence the successful outcome of caudal anesthesia in 29.5 per cent of the cases. These abnormalities consisted of the following: (1) complete agenesis, 3.8 per cent; (2) severe partial agenesis, 8.6 per cent; (3) hiatus absent, 7.7 per cent; (4) hiatus of less than 8 mm. in length, 3.8 per cent; (5) bony septum in canal, .9 per cent; (6) angulation distortion of sacrum, 2.8 per cent; and (7) severe infection without symptoms, 1.9 per cent.

Of the 104 specimens, 15.3 per cent showed defects which made successful caudal anesthesia improbable. In this group were 8 cases of absent hiatus, one case of complete agenesis and bony septum, and 3 cases in which spinal anesthesia appeared inevitable due to angulation distortion.

PATHOLOGY OF PREGNANCY

MISSED ABORTION: AN EVALUATION OF CONSERVATIVE MANAGEMENT

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Am. J. Surg. 2: 77, 1949

The authors present their findings and mode of management of 39 patients with missed abortion. In all the cases the non-viable fetus was retained for a minimum of four weeks.

The ages of the patients varied between 17 and 46 years. The gravidity varied between one and 13. Thirteen patients had previous abortions, an incidence of 33.28%. Seven patients had previous stillbirths, an incidence of 17.9%.

Retention varied from 4 to 28 weeks; 25 (64%) were retained from 4 to 12 weeks; 2 were retained from 12 to 14 weeks; 2 for 14 weeks; 6 were retained for 17 to 20 weeks and 6 were retained for 23 to 28 weeks. It was noted that the period of retention generally varied inversely with the age at which death of the fetus occurred.

Laboratory data indicative of fetal death are not entirely reliable except when the Aschheim-Zondek test is negative and x-ray study indicates positive evidence of death of the fetus.

In 32 patients (82%) the fetus and placenta were expelled completely and no interference was necessary. Five patients required manual removal of the placenta. One patient required a sponge stick removal of retained secundines after rupture of the membranes and passage of some of the gestational contents. Another patient required vaginal pack because of bleeding with an undilated cervix.

Six patients were given stilbestrol or estrogenic hormone therapy to stimulate the spontaneous expulsion of the retained ovum.

From this study of missed abortion the authors believe that a waiting policy is indicated. Spontaneous expulsion of the dead ovum occurs at the time the normal uterine tonus is restored and normal uterine contractions, either alone or with the aid of oxytocic drugs, prevent excessive bleeding.

(In view of the frequent importunities of patients and their relatives for interference in cases of missed abortion, the desirability of a waiting policy, as stressed by the authors, needs continual reemphasis. To go in on these cases is a fairly certain way of getting into trouble—Ed.)

and lung circulation, decreasing the chances of pulmonary complications. Perhaps the greatest reward, however, is the often stated sense of well being on the part of the patient.

Results of early ambulation in gynecology are almost parallel to those in obstetrics. Patients who have been operated upon are permitted to follow the same routine as obstetric patients. Increase in circulation of the extremities, and in the abdominal wall and pelvic contents, has been a large factor in preventing a great many of the common complications and discomforts following operations. Gas pains, distention, nausea and vomiting have practically become something of the past. There has been noted a marked reduction in the amount of sedation needed for patients who are allowed early rising.

Contraindications to early ambulation are few. It is felt that a patient with a temperature of 101 degrees F. or over should not be allowed out of bed, at least not until the cause is known. On the contrary, some physicians feel that walking may help to reduce the fever. Hemorrhage, although rare, is certainly a reason for keeping the patient quiet. There is great difference of opinion about patients who have undergone surgical repair, at childbirth or as a separate operation. It is reasonable to believe that in some instances early ambulation might cause sufficient increase in abdominal force to break down a repair of herniation through the vagina.

While patients who have been permitted early ambulation can safely leave the hospital several days earlier than they might otherwise, complications such as thrombosis, infections and wound separations do occur in such patients, and for that reason they should remain in the hospital under observation until these dangers are past. Moreover, patients should be warned against too vigorous exercises and against doing too much until the body has had time to recover and wounds are safely healed.

cose and vitamins. Although the condition is very rare, its prognostic importance is such as to warrant routine retinal examination in all cases of hyperemesis as originally recommended by Stander. Ballantyne has emphasized other ocular changes in hyperemesis, such as slight dimness of vision to varying degrees of involvement of the visual fields, which may precede gross hemorrhage and optic neuritis and has pointed out that the early recognition of these ocular complications may be of substantial aid in prognosis (*J. Obst. & Gynaec. Brit. Emp.* 48: 206, 219, 1941).—Ed.)

VALUE OF SOYBEAN TRYPSIN INHIBITOR IN PREVENTING THE TOXIC EFFECTS OF HUMAN PLACENTAL THROMBOPLASTIN

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Proc. Soc. Exper. Biol. & Med., 68: 596-598, (July-Aug.) 1948

In 1914, Gaifami demonstrated that saline extracts of the human placenta, injected intravenously, are lethal to animals. Gizelt showed the presence of thromboplastin in the human placenta. Schneider has concluded that the toxicity of placental extracts is entirely attributable to the thromboplastin content. He demonstrated that heparin, added to the extracts *in vitro*, neutralizes the "placental toxin."

These facts have certain clinical implications pertaining to the origin of at least a part of the eclamptic syndrome in women. In eclampsia, the liberation of placental thromboplastin into the maternal circulation might well account for the deposition of fibrin observed especially in the liver. Preliminary reports indicate that heparinization may be of value in the treatment of pre-eclampsia. On the other hand, there are several disadvantages to the clinical employment of heparin over a long period of time.

Macfarlane, utilizing a crystalline soybean trypsin inhibitor, showed that this protein inhibited the coagulation of blood by a "depression of the activity of thromboplastin." The present study was undertaken to determine whether soybean trypsin inhibitor (STI) would protect against lethal effects of human placental extracts.

When given intravenously to 30 mice, STI, in doses equivalent to 0.5 g/kg body weight, was devoid of any apparent toxic or anaphylactic effect. STI was also given intravenously to a guinea pig and to a rabbit (0.5 g per kilo) and 0.25 g/kg to a Rhesus monkey. In these, no apparent toxic or anaphylactic effects were noted. In the monkey, it was observed that the material caused a prolongation of the plasma coagulation time. The lethal dose of human placental thromboplastin solution (HPT) was given to 28 mice, all of which died within 3 minutes. The STI solutions were given intravenously to 24, intramuscularly

HYPEREMESIS GRAVIDARUM WITH
RETINAL HEMORRHAGE

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Am. J. Obst. & Gynec., 57: 589-591, March, 1949

There is very little in the medical literature concerning the association of hemorrhagic retinitis and severe vomiting of pregnancy. The authors have reported such a case and make a plea for more careful ophthalmoscopic examinations in all the toxemias of pregnancy.

The case reported is that of a 34-year-old white gravida ii, para i, who first began to vomit in her fourth week of pregnancy. The vomiting occurred daily but followed no regular pattern and was associated with nausea. She received the classical treatment for 2 weeks without any improvement in her symptoms. On admission to the hospital she was markedly dehydrated and partially comatose. Ophthalmoscopic examination showed advanced diffuse hemorrhagic retinitis obscuring the discs and vessels. The blood count showed 4.0 million red blood cells with 9.1 gms. of hemoglobin.

Interruption of the pregnancy was advised as soon as the severe malnutrition and dehydration could be combatted. She was given large amounts of intravenous fluids, and within 24 hours the hemorrhagic retinitis had cleared except for slight peripheral congestion. Twenty-four hours later, however, after first showing some clinical improvement, the comatose state recurred and the hemorrhagic retinitis reappeared. At this time the uterus was emptied under light pentothal anesthesia. Intravenous fluids were continued postoperatively, and over the next several days the patient showed clinical improvement and there was gradual return of vision. On subsequent follow-up visits she exhibited no residual ocular or cardio-vascular-renal disease.

The authors have expressed the opinion that the ocular hemorrhages are due to increased capillary permeability secondary to the dehydration and inanition. These changes are felt to be entirely reversible if prompt treatment is carried out. In this case, prompt termination of pregnancy resulted in complete recovery.

(Back in 1931 we happened to have in rapid succession 2 cases of hyperemesis with retinal hemorrhage in our clinic which were reported in detail by Stander in Surg., Gynec. & Obst. 54: 129, 1932. One of these patients died despite therapeutic abortion. Two years later Tillman reported 3 cases from the Sloane Clinic, of which 2 were fatal (Am. J. Obst. & Gynec. 27: 240, 1934). In a review of the literature, omitted from the above abstract, Evans and Kannapel state that their case makes a total of 12 so far reported with 8 deaths, a mortality of 75 per cent. Although it has been suggested that retinal hemorrhage in hyperemesis is a sign of vitamin B complex deficiency, the reported cases indicate that retinal hemorrhage is seen only in the most advanced stages of hyperemesis and it is the consensus that the finding constitutes an urgent indication for interruption of pregnancy after the patient has been put in as good condition as possible by means of intravenous fluids, glu-

festated by renal hypertrophy and nephritis in a number of these animals. Both renal hypertrophy and nephritis are consistently intensified by the concomitant administration of DCA. Hypertension develops in both pregnant and non-pregnant rats treated with anti-placenta serum employed together with the daily administration of DCA. Termination of pregnancy, in the face of continued DCA administration, fails to lower the blood pressure or to arrest the nephritic process.

(Here again we find modern biological methods brought to the old riddle of eclampsism by another group of competent investigators. Because of its relationship to salt metabolism and water balance, it is widely suspected that desoxycorticosterone may have something to do with the toxemias and the findings in this paper tend to support that viewpoint.—Ed.)

ANAEMIA SIMULATING PRE-ECLAMPTIC TOXAEMIA

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J. Obst. & Gynaec. Brit. Emp., 56: 28-35, February, 1949

The authors describe 13 cases of anemia of pregnancy simulating pre-eclamptic toxemia. All of the patients were under 30 years of age except the 4 very severe cases, whose ages ranged from 36 to 39 years. Almost all the patients lived in poor economic circumstances. In the majority of cases, no complaint referable to anemia was made although all cases had hemoglobins below 8 g. per cent. In the 4 most severely anemic patients, whose hemoglobin was less than 5.1 g. per cent, the general symptoms of anemia were present.

The striking feature in all cases was the presence of signs usually associated with pre-eclamptic toxemia. Edema was present in all cases and appeared to be proportional to the degree of anemia. The blood pressure was elevated in all cases, the readings ranging from 170/100 to 140/80. The systolic pressure was relatively higher than the diastolic, with a consequent increase in pulse-pressure. With the exception of 2 patients who had pyuria due to a coliform infection and a third patient who had tracheitis in addition to a very severe anemia, only a trace of albumin could be found in the urine. Trophic changes were common when the anemia was very severe.

Prenatally, the syndrome can be distinguished from that of true toxemia by careful examination of the blood pressure, urine and blood picture. The true diagnosis becomes apparent after admission to the hospital, when changes occur in the blood pressure and albuminuria. The blood pressure usually falls to normal limits within 24 to 48 hours after admission, and the urine rapidly clears with rest in bed.

to 18 and subcutaneously to 10 animals. The intravenous injection of the soybean material prevented any reactions to lethal doses of HPT in 88 per cent of the group. The intramuscular route offered moderate protection provided that 2 hours elapsed before giving the HPT, 72 per cent of the group showing no reaction. The subcutaneous route was least effective, with 50 per cent of the animals showing immediate reaction and 50 per cent delayed reaction to HPT.

When the STI and HPT solutions were incubated *in vitro* before injection, there was almost complete neutralization of the toxic effects.

(As the authors point out, the idea that a placental thromboplastic substance may play an important role in the mechanism of eclampsia dates back to the early years of the century. By the employment of modern chemical and biological methods, Page, Schneider and others have done much to document this old theory and today it stands in the limelight to a greater extent possibly than at any previous time. It will be noted that the 64 million dollar question is now being tackled, namely: can a specific cure for eclampsia be evolved on the basis of this theory? Hence the importance of this paper.—Ed.)

OBSERVATIONS ON THE PREGNANT RAT INJECTED WITH NEPHROTOXIC RABBIT ANTI-RAT PLACENTA SERUM AND DESOXYCORTICOSTERONE ACETATE

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J. Exper. Med., 89: 287-293, March 1, 1949

It has been suggested that a toxemia of pregnancy may result from the action of injurious antibodies evoked by antigenic substances of placental origin. The injection of rabbit anti-rat placental serum into pregnant rats regularly produces abortion and subsequently a large number of these rats will develop chronic glomerulonephritis. The present experiment was undertaken to determine if the addition of salt and desoxycorticosterone acetate would, in addition to producing abortion, also cause toxemia.

Pregnant and non-pregnant rats were given the anti-placenta serum and in addition one-half of the rats in both groups were also given sodium chloride and desoxycorticosterone acetate (DCA). Hypertension occurred in both the pregnant and non-pregnant rats which received DCA. Albuminuria was present in the groups receiving serum and those receiving DCA. Progressive cardiac enlargement occurred in those receiving DCA and renal enlargement also was seen in this group. Chronic nephritis was found on histological examination in the rats receiving serum and DCA more frequently in the pregnant group.

The authors conclude that pregnancy enhances the susceptibility of the rat to intercurrent renal damage produced by anti-placental serum. This is mani-

per cent syphilitic infants. There is no question that penicillin therapy is the method of choice.

The penicillin treatment is virtually reactionless. The whole treatment of the mother can be given during the pregnancy and can be completed in a few days. Penicillin permeates the placenta to the fetus in what appears to be therapeutically effective amounts.

Prior to the use of penicillin, a woman with primary or secondary syphilis in the last 2 months almost invariably gave birth to an infected child. Now treatment in the last few weeks of pregnancy results in a normal infant, occasionally seropositive and reaching sustained negativity without additional therapy.

A negative maternal blood test at the time of delivery is not a requisite for obtaining a healthy nonsyphilitic infant, since the average period required to reach seronegativity is 245 days and many mothers are treated in the last months of pregnancy. Penicillin, in curing at least 70 per cent of the mothers, has accomplished more than any other treatment. A single course of penicillin treatment during pregnancy and monthly physical examinations and quantitative titered blood serological tests thereafter are usually sufficient to protect the fetus. Retreatment prior to delivery is to be considered if the mother fails to show a normal response.

In the medical follow-up of the infant the serologic status at birth must be determined. However, the author found that only 7.3 per cent of the seropositive infants had syphilis. The following criteria in addition to positive dark-field examination of the skin lesions may be used: 1, a titer of syphilitic reagin in the infant higher than that in the mother; 2, a high sustained or increasing titer during the first month of life; 3, a positive serologic test after three months; 4, unequivocal roentgenographic signs of osteochondritis or periostitis during the first 3 months.

The infant while in the nursery should have a complete appraisal for syphilis. A seropositive infant should have the blood test repeated every 2 weeks and the roentgenogram repeated at 6 weeks. The seronegative infant should have blood tests at 1, 2, 3, and 6 months. If no evidence of syphilis has been observed after 6 months no infantile congenital syphilis is present.

Satisfactory dosage of penicillin to prevent congenital syphilis consists of 2.4 million units or more given over a period of 7 days. There would seem little reason to add arsenic or bismuth to this regimen. There is not much choice between aqueous penicillin and penicillin in oil and beeswax. A possible exception occurs in the case of early syphilis in late pregnancy when the fetus is most likely to be infected already and it is necessary to maintain a sustained high level of penicillin in the mother. Here aqueous penicillin is most effective. A full dosage may be given from the start.

The question of retreatment in subsequent pregnancies of the woman who has had a standard course of penicillin for syphilis prior to conception is difficult to answer. However, various reports show that the number of syphilitic infants born in this group is extremely small, less than one per cent when no retreatment was given. If it is decided to withhold treatment it is necessary that the patient

It is pointed out that the absence of symptoms and objective signs referable to anemia would appear to be related in some measure to the increased blood pressure and the consequent increased rate of circulation. This hypothesis seems to hold for all anemias. A series of 104 anemias in pregnant patients has been surveyed and has shown that the presence or absence of symptoms varied directly with the blood pressure level.

Untreated asymptomatic cases rapidly became symptomatic in the puerperium, generally about the third day. At this time hemodilution was most marked and the blood pressure had previously fallen with the rest in bed. The sudden appearance of symptoms in these cases may afford an explanation for reports appearing in the literature of cases of puerperal pernicious anemia of sudden onset.

Examination of the peripheral blood and bone-marrow has shown that these are cases of a typical pernicious anemia of pregnancy. The peripheral blood picture is that of ordinary iron deficiency anemia, but the bone-marrow contains megaloblasts and the normoblasts are greatly reduced.

The diagnosis of pernicious anemia of pregnancy is confirmed by the response of these cases to treatment in the prenatal period. Iron therapy rectifies the iron deficiency, but no improvement in the blood picture occurs beyond a certain limit, generally, 8 g. per cent. At this level liver therapy has to be provided before any improvement is obtained. In the puerperium, iron alone is sufficient to raise the blood values to normal, but therapy must be prolonged.

(As seen in the Orient, the severer degrees of pernicious anemia of pregnancy are regularly associated with edema of nutritional origin and sometimes the edema is massive. In the very advanced cases, with hemoglobin concentrations around 3 grams, heart failure occasionally occurs, due presumably to anoxia of the myocardium. These are often very sick women and show sundry morbid processes, especially obscure infections and fever, but hypertension has not been stressed in such cases prior to the noteworthy observations recorded above. Since the blood pressure falls so promptly on bed rest, it is barely possible that it is cardiac in etiology.—Ed.)

PRENATAL MANAGEMENT OF SYPHILIS WITH SPECIAL REFERENCE TO PENICILLIN THERAPY

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M. Clinics North America 32: 1647-1658, (November) 1948

In a total of 580 cases from published reports, the infant has been followed sufficiently to determine the value of the treatment of the pregnant syphilitic with penicillin to prevent congenital syphilis. The women studied had primary, secondary or early latent syphilis. A living syphilitic infant was born in only 2 per cent of the cases. The application of arsenic and bismuth results in 5 to 7

Thirty-two of the 39 pregnancies have resulted in normal, living nonsyphilitic infants. Six patients went into premature labor during penicillin therapy and 2 of their children were born with congenital syphilis. One patient developed a serologic relapse prior to parturition and delivered a syphilitic child. There were 4 infant deaths, 2 of which were probably caused by syphilis. It has been estimated that arsenical therapy in patients such as these would result in about 15 to 20 per cent of the children having congenital syphilis. The reports of other workers using amorphous penicillin showed approximately 6 per cent fetal deaths probably not related to syphilis and 4 per cent syphilitic infants. These results are somewhat superior to those in the present series, but it should be emphasized that 35.9 per cent of the authors' patients were treated in the last 8 weeks of pregnancy. Six patients have had subsequent pregnancies and delivered normal infants; it is apparent that treatment with penicillin may protect the mother and baby in subsequent pregnancies.

DIABETIC FERTILITY, MATERNAL MORTALITY, AND FOETAL LOSS RATE

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Brit. M. J., 1: 48-51, January 8, 1949

It is apparent that the introduction of insulin has increased the fertility of diabetic women. While the fertility rate among 190 diabetic women between 1893 and 1922 was 2 per cent, Skipper (1933) noted a fertility rate of 15 per cent among 177 diabetic women between 1923 and 1931, and Eastman (1946) observed a fertility rate of 28.6 per cent. Similarly, the rate of diabetic to non-diabetic pregnancies admitted to large obstetric hospitals has risen. Williams (1909) saw only one pregnant diabetic in his 13 years in charge of the obstetric service at Johns Hopkins Hospital, whereas at the Simpson Memorial Maternity Pavilion of the Royal Infirmary, Edinburgh, between 1943 and 1947, the ratio was 1 in 292.

The advent of insulin has also made pregnancy relatively safe for diabetic women. An immediate maternal mortality of between 25 and 30 per cent in diabetic women was associated with pregnancy in the pre-insulin era. A mortality rate of less than 2 per cent was quoted by Lawrence and Oakley (1942) and several smaller series of cases have revealed no maternal loss. There was one maternal death among the 70 diabetic pregnancies at the Simpson Memorial Maternity Pavilion between 1942 and 1947.

However, insulin therapy has failed to produce a very significant decrease in the fetal mortality rate in diabetic women. Henley (1947) noted a fetal loss

be followed carefully until term. A rational standard for withholding treatment would be as follows: 1, the woman was treated for early symptomatic syphilis and had a normal clinical and serological response; 2, the woman was treated for latent syphilis and maintained a negative spinal fluid and became seronegative or retained; 3, the woman was treated for symptomatic late syphilis and sustained a normal response.

When an infant with congenital syphilis results, failure of the penicillin treatment as such can almost never be blamed.

(A succinct summary of the several advantages of penicillin therapy in syphilitic pregnant women by one of the leading authorities of the country.—Ed.)

THE USE OF CRYSTALLINE PENICILLIN G IN THE TREATMENT OF SYPHILIS IN PREGNANCY

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Am. J. Obst. & Gynec., 57: 461-465, March, 1949

The results of this study indicate that crystalline penicillin G is of considerable value in the prevention of congenital syphilis, even when given late in pregnancy. Thirty-nine pregnant women with early syphilis were treated. The diagnoses of these patients at the time of treatment were as follows: seropositive primary syphilis, 2 cases; secondary syphilis, 25 cases; recurrent syphilis, 2 cases; and early latent syphilis, 10 cases. None of the patients had had treatment for syphilis except the 2 patients with recurrent secondary manifestations. Twenty patients were treated between the 16th and 32nd weeks of pregnancy; 14, after the 32nd week; while only 5 began their treatment before the 16th week.

Treatment consisted of a total dose of 4.8 million units of crystalline penicillin G to each patient. This was given in doses of 80,000 units every 3 hours for 60 injections in 7½ days. No additional therapy was administered. Quantitative serologic tests were carried out at monthly intervals after treatment. Serologic tests for syphilis were taken on both mother and child at delivery, at monthly intervals thereafter for 6 months, and then every 2 or 3 months. Careful physical examination of the child was performed at birth and roentgenographic examination of the long bones was made.

Thirty-four of the 39 patients treated for syphilis in pregnancy have obtained a satisfactory clinical and serologic response. The lesions disappeared promptly in these patients, and no evidence of recurrence has been noted. Thirty-two of them now have a negative serologic test. Five patients have developed evidence of treatment failure following penicillin therapy. In 4 cases the children were not infected.

from those in the insulin group. There seems, therefore, to be no relation between the severity of the ensuing diabetes and the pre-diabetic fetal loss rate.

The similarity of the fetal loss rate in the immediate pre-diabetic phase and in the post-diabetic period raises a doubt whether the immediate pre-diabetic period is in fact pre-diabetic. The authors feel that there is a factor conducive to fetal mortality which may be active for as long as 20 years before the diagnosis of diabetes and very active for the immediately preceding 5 years. It is considered probable that the factors responsible for the large babies, high fetal loss rate and the ensuing maternal diabetes have a common basis in some general metabolic disturbance in the mother, and that the features of clinical diabetes (polyuria, glycosuria, thirst, etc.) are a very late stage of this metabolic disturbance, an early feature of which is a high fetal loss rate.

(This is one of the most thorough studies which have been made of fetal mortality in prediabetic women. It concurs with previous investigations in showing that there is some unknown factor conducive to fetal mortality which may be active in these women for as long as 20 years before the diagnosis of diabetes is made; and, for the immediate preceding 5 years, it may be very active. On the basis of the similarity of the fetal loss rate in the immediate prediabetic phase and in the postdiabetic, plus the fact that the severity of the disease is not related to the fetal mortality, the authors (as I understand them) quite rightly raise the question as to whether it is actually diabetes per se which is basically responsible for these infant deaths. The concluding sentence of the abstract, following along in the same vein, is most thought-provoking. And indeed, this is a curious enigma.—Ed.)

PREGNANCY COMPLICATED BY DIABETES MELLITUS

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Brit. M. J., 1: 51-54, January 8, 1949

A series of 45 patients with diabetes mellitus have been observed through 58 pregnancies in the past 20 years at the University College Hospital. The incidence was one in 580 deliveries. This high figure was due to the number of referred patients from the Diabetic Clinic. In 48 of the pregnancies diabetes had been diagnosed before the onset of gestation; in the remaining 10 cases the diagnosis was made during pregnancy and confirmed after pregnancy. Thus, in about $\frac{1}{4}$ of the patients pregnancy appeared to unmask the diabetic condition.

Fifty-one pregnancies were treated with insulin and 7 by diet alone. Of 19 cases under insulin treatment in which the diet remained unchanged, 9 required more insulin as pregnancy advanced up to the time of delivery, 9 required more up to 2 to 4 weeks before delivery, and the remaining patient needed no alteration in insulin dosage throughout pregnancy. Seventeen of the 19 patients showed a marked fall in insulin requirements after delivery. These

of 43 per cent in 169 pregnancies during the pre-insulin era, compared with 37.6 per cent in 924 pregnancies since the introduction of insulin. The fetal loss rates for the whole course of pregnancy and the neonatal period reported by other writers were 64, 43, 44 and 37 per cent. In the present study, the term "fetal loss rate" means percentage of all pregnancies not resulting in the birth of a baby living for at least 14 days. By this definition, the authors' fetal loss rate during the last 5 years has been 51.4 per cent.

These figures are in striking contrast to recent results published by White (1946). Using hormonal therapy to correct abnormal gonadotrophin and pregnanediol levels, she found a fetal loss rate of only 3 per cent when hormonal levels were normal in comparison to 48 per cent in cases with abnormal hormonal levels; but correction of abnormal levels lowered the fetal loss rate to 10 per cent. Her series did not include abortions before the 24th week of pregnancy, but the fetal mortality reported by White is incomparably lower than in any other large series of cases.

In the present study, 165 consecutive parous diabetic women (aged 25 to 69 years) were interviewed personally and their pre-diabetic histories analyzed. As control material, obstetric histories of 1,027 women admitted to the Ayre County Maternity Service in 1942 were analyzed. Among the 3,276 pregnancies involved there was a fetal loss of 263 (8 per cent). The components of the fetal loss rate were: abortions and miscarriages, 2.8 per cent; stillbirths, 3.2 per cent; deaths occurring in the first 14 postnatal days, 2 per cent.

The 165 diabetic patients studied were divided into 2 main groups: (1) insulin group—132 women in whom insulin therapy was necessary for control of the disease; (2) non-insulin group—33 patients in whom dietary treatment alone was sufficient for diabetic control. Each of these groups was subdivided into (a) young diabetics—women in whom diabetes was diagnosed before the age of 45; and (b) old diabetics—women in whom the disease was diagnosed after the age of 45.

The overall fetal loss rate in the 132 pre-diabetics who were taking insulin was 15.7 per cent, or twice the non-diabetic control rate of 8 per cent. The fetal loss rate steadily reaches a maximum in the 2 years immediately before the diagnosis of diabetes, when the fetal loss rate was 50 per cent. This was 6 times the control rate, and was as high as that observed after the onset of clinical diabetes.

The pre-diabetic overall fetal loss rate among 59 young diabetics requiring insulin was 24.2 per cent, or 3 times the control rate. The overall fetal loss among 73 old diabetics requiring insulin was 12.5 per cent in 335 pregnancies. None of these women had been pregnant for at least 4 years before the onset of their diabetes.

The patients requiring only dietary treatment for diabetic control form a small group of 6 young diabetics and 27 old diabetics. The overall fetal loss rate of 14.5 per cent in this group is not significantly different from the rate of 15.7 per cent in the women requiring insulin. Subdivision of the non-insulin group into young and old diabetics reveals fetal loss rates not significantly different

from those in the insulin group. There seems, therefore, to be no relation between the severity of the ensuing diabetes and the pre-diabetic fetal loss rate.

The similarity of the fetal loss rate in the immediate pre-diabetic phase and in the post-diabetic period raises a doubt whether the immediate pre-diabetic period is in fact pre-diabetic. The authors feel that there is a factor conducive to fetal mortality which may be active for as long as 20 years before the diagnosis of diabetes and very active for the immediately preceding 5 years. It is considered probable that the factors responsible for the large babies, high fetal loss rate and the ensuing maternal diabetes have a common basis in some general metabolic disturbance in the mother, and that the features of clinical diabetes (polyuria, glycosuria, thirst, etc.) are a very late stage of this metabolic disturbance, an early feature of which is a high fetal loss rate.

(This is one of the most thorough studies which have been made of fetal mortality in prediabetic women. It concurs with previous investigations in showing that there is some unknown factor conducive to fetal mortality which may be active in these women for as long as 20 years before the diagnosis of diabetes is made; and, for the immediate preceding 5 years, it may be very active. On the basis of the similarity of the fetal loss rate in the immediate prediabetic phase and in the postdiabetic, plus the fact that the severity of the disease is not related to the fetal mortality, the authors (as I understand them) quite rightly raise the question as to whether it is actually diabetes per se which is basically responsible for these infant deaths. The concluding sentence of the abstract, following along in the same vein, is most thought-provoking. And indeed, this is a curious enigma.—Ed.)

PREGNANCY COMPLICATED BY DIABETES MELLITUS

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Brit. M. J., 1: 51-54, January 8, 1949

A series of 45 patients with diabetes mellitus have been observed through 58 pregnancies in the past 20 years at the University College Hospital. The incidence was one in 580 deliveries. This high figure was due to the number of referred patients from the Diabetic Clinic. In 48 of the pregnancies diabetes had been diagnosed before the onset of gestation; in the remaining 10 cases the diagnosis was made during pregnancy and confirmed after pregnancy. Thus, in about $\frac{1}{4}$ of the patients pregnancy appeared to unmask the diabetic condition.

Fifty-one pregnancies were treated with insulin and 7 by diet alone. Of 19 cases under insulin treatment in which the diet remained unchanged, 9 required more insulin as pregnancy advanced up to the time of delivery, 9 required more up to 2 to 4 weeks before delivery, and the remaining patient needed no alteration in insulin dosage throughout pregnancy. Seventeen of the 19 patients showed a marked fall in insulin requirements after delivery. These

figures support the contention that carbohydrate tolerance usually diminishes as pregnancy advances. However, in 9 patients carbohydrate tolerance increased prior to delivery. Eight of the 9 patients were receiving estrogen therapy at the time, and it is felt that this may have been a factor in the improvement.

The marked and abrupt fall in insulin requirements after delivery in the majority of patients must be emphasized, because of danger of hypoglycemic coma if this fact is neglected.

The tendency of the pregnant diabetic to develop hydramnios is confirmed by the fact that clinical hydramnios developed in 17 of the pregnancies in this series, an incidence of 29 per cent.

It was found that hypoglycemic symptoms and coma tend to occur early in pregnancy, and ketosis and diabetic coma in the latter part of pregnancy. In some patients ketosis was precipitated by the onset of urinary infection. The hypoglycemic symptoms noted in early pregnancy may have been related to the development of renal glycosuria, often found in normal pregnancy, or to the prevalence of hyperemesis in early pregnancy, or to insulin overdosage.

There is a greater tendency for the diabetic to develop late pregnancy toxemia than the non-diabetic, and the relative incidence varies with the standard of severity of the toxemia taken for comparison. On the strict standards for classification of late pregnancy toxemia adopted at this hospital, there were 25 diabetic pregnancies with this complication, an incidence of 43 per cent. The toxemia in 12 of the 25 cases was severe enough to warrant hospital admission, or an incidence of toxemia of this severity of 20.7 per cent.

The maternal prognosis in diabetic pregnancy is good, and pregnancy does not make the diabetes worse provided that it is well treated. There was one immediate death in the present series. Four pregnancies were followed by puerperal pyrexia; 2 were due to urinary infection, one to pleurisy and one probably due to puerperal sepsis. In 34 pregnancies the carbohydrate tolerance before and after pregnancy is known; in 28 (82 per cent) it was unchanged and in 6 it was decreased. The onset of diabetes in these 6 patients occurred within a few months of the beginning of pregnancy or during the pregnancy.

The obstetrical histories of the patients in the present series show that of 64 diabetic pregnancies, 7 ended in abortion, an incidence of 10.9 per cent. It would seem that the incidence of abortion is no greater in the pregnant diabetic than in the non-diabetic. The high fetal mortality in the pregnant diabetic is therefore due to some unknown factor which causes death of the viable fetus and newborn infant. The late fetal mortality was 55 per cent in a first series of 43 pregnancies. In a second series of 15 pregnancies in which estrogens were given there were only 3 deaths. It is suggested that the factor affecting the viability of the fetus probably arises in the maternal anterior pituitary lobe.

Congenital deformities, gigantism and hypoglycemia of the newborn are briefly discussed, and it is suggested that the tendency to gigantism is due to an excess of the growth hormone in the maternal pituitary gland.

(The above paper, which incidentally appeared in the same issue of the British Medical Journal as the preceding one by Gilbert and Dunlop, is replete with instructive clinical facts. I am particularly interested to note that the incidence of abortion in this series

was but 10.9 per cent. Diabetes is sometimes cited as a cause of abortion, but after analyzing a few years ago the actual figures given in various series of cases, I reached the conclusion that the abortion rate in these women is little if any raised above the incidence in nondiabetic patients, namely, 10 per cent; and I am pleased to see that Barnes and Morgans agree. The authors' statement that hypoglycemic symptoms and coma tend to occur early in pregnancy, whereas ketosis and diabetic coma are more prone to occur late, is a new observation as far as I am concerned, but looking back on past cases I am inclined to believe it is a correct one.—Ed.)

PREGNANCY COMPLICATED BY PRIMARY TORSION OF A NORMAL FALLOPIAN TUBE

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Virginia M. Monthly, 76: 127, March, 1949

The case is reported of a 24-year-old female who was admitted to the Winchester Memorial Hospital because of a pregnancy (7 months) complicated by pain in the right lower quadrant. The pain was of 36 hours' duration but had been acute for only 12 hours prior to admission. On examination, the patient was unable to lie flat because of the pain. There was acute tenderness in the right lower quadrant with associated muscle spasm. The uterus was normal to examination. The temperature was 99 degrees F. The white blood count was 11,050.

At operation, the right Fallopian tube was found to be twisted, gangrenous and distended with serosanguineous fluid. The right ovary and appendix were normal. A right salpingectomy was done and the patient made an uneventful recovery. The appendix and ovary were not removed as it was believed that a minimal amount of operative intervention would be less likely to precipitate a premature labor. The patient delivered a normal living child at term.

(See editorial note following next abstract.—Ed.)

TORSION OF THE NORMAL FALLOPIAN TUBE COMPLICATING PREGNANCY: REPORT OF A CASE

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New England J. Med., 240: 421, March 17, 1949

A case is reported of a 23-year-old primigravida who was admitted to the hospital complaining of intermittent right anterior abdominal pain of 11 days'

duration and urinary frequency of 3 days' duration. One day before admission, right lower quadrant tenderness was noted for the first time. The patient was in her fifth month of pregnancy and prior to the present complaint her course had been uneventful, except for mild morning sickness. Examination was negative except for the right lower quadrant tenderness. The white blood count was 11,600. A laparotomy was performed and a dark mass was found beneath the right ovary. This mass was untwisted and found to consist of the terminal $\frac{2}{3}$ of the fallopian tube. The involved portion of the tube was removed and the abdomen was immediately closed. The postoperative course was uneventful and the pregnancy progressed normally. Pathologic examination of the tube showed congestion and hematosalpinx which were felt to be secondary to the torsion.

The author feels that acute appendicitis, ovarian cyst with a twisted pedicle, ectopic pregnancy and hydrosalpinx must be included in the differential diagnosis of this rare condition.

(A considerable literature has appeared during the past few decades, largely in the form of case reports, upon the subject of torsion of the fallopian tube. While this anomaly, particularly torsion of a hydrosalpinx, has long attracted widespread interest and has elicited sufficient study, it would seem, to establish it on a clearcut basis, a review of the newer case reports and the discussions appending them reveals two noteworthy discrepancies in our knowledge of the subject: (1) a noticeable variation appears in the stated frequency of the condition, some writers considering it of the rarest occurrence, while others believe it "not uncommon"; (2) an increasing number of cases are being reported as torsion of the normal fallopian tube, as for example in the above 2 case reports. Does torsion of the normal tube occur, or do supposed instances of this represent, as the earlier writers insisted, examples of torsion of an already existing hydrosalpinx?

In regard to the frequency of torsion of tubal enlargements in general, approximately 100 cases had been reported as far back as 1927. That the true incidence is higher than this figure would indicate is suggested by several facts. Of particular interest in this regard is the frequency with which individual operators have met and recorded two or more cases: one man has reported 8, another 5, several 3, etc. Not only is this an argument against the rarity of the condition, but it suggests the possibility that individual cases have not been reported because it did not seem worthwhile to report single cases when several writers had already reported meeting multiple ones. Moreover, commentators on case reports have frequently referred to one or more cases which they had encountered but had not recorded. A good many years ago I happened myself to meet 3 cases of torsion of hydrosalpinges in rather rapid succession and am convinced that the accident, although uncommon, can scarcely be regarded as rare (*Surg., Gynec. & Obst.* 45: 143, 1927).

A large number of cases of torsion of the fallopian tube have been reported, of course, since 1927 and in many instances they have been described as torsion of the normal fallopian tube. The question arises: which cases, if any, represent torsion of normal tubes and which torsion of hydrosalpinges? While in many cases this is easy to answer, in some it is impossible. Writers who insist that torsion of normal adnexa does occur support their attitude on the ground that many of the cases are seen in virgins and particularly in girls of puberty age in whom an already existing hydrosalpinx would seem unlikely; moreover, at operation no adhesions or evidence of other antecedent pathological changes were found. The earlier writers, particularly Anspach, hold to the view that in such cases the tube is the seat of a hydrosalpinx before torsion and that it is converted into a hematosalpinx as the result of twisting. They explained the existence of a hydrosalpinx in virgins and in patients who give no history of pelvic inflammation on the following basis: (a) it may occur as a sequel of vulvovaginitis in childhood which persists in latent form until puberty and then

produces involvement of the tube which is not recognized; (b) it may be the late result of an unrecognized salpingitis which has occurred in the course of one of the exanthemata; (c) it may be the result of an attenuated tuberculous infection. When it is recalled that unilateral hydrosalpinges are occasionally seen without other pathologic changes and that torsion of a normal fallopian tube immediately produces an identical picture, namely, hydrosalpinx and hematosalpinx, the difficulty of distinguishing between torsion of a hydrosalpinx (in certain cases) and torsion of a normal tube becomes apparent. In either instance the operative findings might be the same, namely, a massive tubal distention, usually of the ampullary portion of the tube, with hydrosalpinx, hematosalpinx, and a bluish discoloration due to passive congestion. Although various arguments may be adduced to support both sides of the question, no absolute proof or disproof of either contention seems available and the problem remains apparently an open one.

A goodly proportion of the cases reported of torsion of the fallopian tube, possibly 10 per cent, have occurred in pregnant women. Since hydrosalpinges are less likely to be encountered in pregnancy, this fact itself lends some slight support to the viewpoint that the normal fallopian tube may occasionally twist. From a clinical point of view it is worthwhile noting that the clinical picture is much less alarming, as a rule, when the tube rather than the ovary is twisted, but otherwise the signs and symptoms are very similar and the differential diagnosis is seldom made prior to operation.—Ed.)

ABDOMINAL PREGNANCY FOLLOWING RUPTURE OF CAESAREAN SCAR

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Canad. M. A. J., 60: 70-71, (Jan.) 1949

The case is presented of a 25-year-old married woman who was admitted to the hospital on March 14, 1947, because of failure to deliver 11 months after the onset of her pregnancy. Two years previously she had been delivered at 7 months by cesarean section. The present pregnancy had been entirely uneventful until 2 months prior to admission when she experienced colicky lower abdominal pains which occurred at 5-minute intervals and were interpreted as labor pains. The pains continued for 3 days and there was neither show nor vaginal bleeding. Fetal movements ceased at that time but abdominal pains severe enough to keep her in bed persisted for 5 weeks. Vaginal bleeding began 2 weeks after cessation of fetal movement and persisted until admission.

On examination an abdominal tumor was palpated which extended 3 cm. above the umbilicus. Fetal poles and fetal heart were not identified. The cervix was soft and the uterine body could not be made out. The mass was felt on pelvic examination only by abdominal counter pressure. The Friedman test was negative and x-ray showed a dead fetus lying transversely in the abdomen. The bleeding stopped on bed rest, and the patient refused laparotomy and so was discharged.

For the first 8 months after discharge her menstrual history was normal.

Subsequently, vaginal bleeding and discharge began again. These were accompanied by chills, fever, general malaise, headache and abdominal pain, so that the patient sought readmission. On examination a globular crepitant mass was palpated in the lower left quadrant in addition to the abdominal mass. The cervix was small and retracted up under the symphysis. A laparotomy was performed and the fetus was found covered with a thick fibrous capsule with the bowel and omentum adherent to this capsule. The mass was dissected free and was found to be attached to a gaping classical cesarean scar. The uterine musculature was very friable, so a supravaginal hysterectomy was performed. The fibrous mass was opened and found to contain the softened skull and skeleton surrounded by an amorphous mass of tissue. No remnants of the placenta were found. The postoperative course was uneventful and the patient was discharged in good condition.

The author points out that often the reattachment of the placenta to major organs creates a real problem if these cases are operated immediately. He feels that if the patient's condition warrants it, it is often wise to wait several months until the placenta is resorbed.

(This is a case of great interest although the designation "abdominal pregnancy" is scarcely in keeping with the usual connotation of that term. By abdominal pregnancy is meant peritoneal *implantation* of the fertilized ovum. It is true that such implantations are almost always secondary, but in Karsh's case there is no evidence that secondary implantation occurred, since the infant promptly died, and furthermore, secondary implantation of a full term placenta is unthinkable.

The case is nevertheless of interest because in the first place the patient, after rupture of a cesarean section scar, carried the fetus in the peritoneal cavity for some 10 months, and secondly, because the placenta was entirely absorbed. This is the first case I have heard of in which (a) an unimplanted placenta was absorbed by the peritoneum and in which (b) the placenta was absorbed in the presence of the fetus.—Ed.)

INTRAUTERINE FETAL DEVELOPMENT IN PROLONGED PREGNANCY

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Geburtsh. u. Frauenhk. 7: 134-146, Dec. 1947

The general impression is that in prolonged pregnancy children of excessive weight and length are produced. This study is based upon 15,101 live births over the course of almost 50 years. The length of the pregnancy and the weight and length of the child were determined in all premature and mature liveborn children from 1901 to 1945. Multiple births and congenital deformities were excluded. The duration of pregnancy was determined by the first day of the last period as stated by the mother.

The average value and the median value for both the weight and the length of the child increase in an exactly similar manner up to 259 days of gestation. The author's tables show that the longer the pregnancy the greater the weight of the child and the greater its length. In pregnancies of over 300 days' duration an especially rapid increase in weight and length could not be demonstrated. The growth curve rises rapidly up to 280 to 300 days but thereafter remains relatively steady. Thus, if the child has achieved a given state of development prolonged pregnancy can no longer cause its weight and length to increase.

Marked differences of the values for weight and length of the child occur in premature pregnancies. This is a clear demonstration of the variation of rapidity of the growth of different children. This variation, however, becomes much less as pregnancy progresses. The closer the child is to term, the more closely do the values for weight and length correspond.

Only in $\frac{1}{10}$ of the cases of prolonged pregnancy did the author find weights and lengths higher than 4000 grams and 55 cm. respectively. The weight and length curves come together at a certain point in pregnancy. In most cases the child thereafter grows no further despite prolonged pregnancy. The development in length is more rapid than the development in weight but this occurs only within the normal time of pregnancy and is no longer observed during prolonged pregnancy. The state of development of the child influences the duration of pregnancy more strongly than does the duration of pregnancy the development of the child.

On the average, the duration of the pregnancy in giant children (length over 57 cm. and weight over 4500 grams) is not increased.

(The observations of the author agree in main with those of Calkins (Am. J. Obst. & Gynec. 56: 167, 1948). In a study of 6000 pregnancies Calkins found that the placenta and baby weights increase rapidly up to about the 260th day. From the 260th to the 280th day weight increase becomes much less rapid and the increment after full term is reached is very small. In Calkins' opinion, if an infant is to be oversize at full term, it will have acquired most of that excessive size by day 260 approximately, whereas if the infant is large at full term, any further increase in size will be of little significance.

There appears to be no agreement in regard to the definition of the term "prolonged pregnancy." In Solth's opinion, it seems to be a pregnancy which lasts over 300 days, whereas Sievers defines it as one which exceeds 294 days in duration, that is, goes 2 weeks or more over the average figure of 280 days (Zentralbl. f. Gynak. 69: 726, 1947). The figure of 295 days was used by Rathbun, in 1943, (Am. J. Obst. & Gynec. 46: 278, 1943) when he discussed the problem as it occurred in the Boston Lying-in Hospital. However this may be, the practical lesson to be drawn from these several studies is that, from the viewpoint of fetal size at least, prolongation of pregnancy need be of no concern to the obstetrician. In other words, as both Rudolph Holmes and Calkins have expressed it, postmaturity is no problem.—Ed.)

TERM PREGNANCY COMPLICATED BY A RUPTURED
APPENDIX WITH GENERALIZED PERITONITIS

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West. J. Surg., 57: 120-122, March, 1949

The truism that a perforated appendix with suppurative peritonitis has a higher morbidity and a greater mortality in the presence of the pregnant than in the non-pregnant woman still stands, as do the well known precepts that the prognosis depends largely upon the rapidity with which the diagnosis is made and the operation performed. Reports in the literature show that the mortality varies between 20 and 70 per cent, depending upon the stage of pregnancy in which the patients are referred for operation and type of treatment instituted.

The writers feel that a modified Porro cesarean section should always be done in the presence of a ruptured appendix with generalized peritonitis. They further believe that if the above procedure is not carried out, the pregnancy can rarely be saved for the following reasons: (1) Labor will follow the operation of a simple appendectomy within a few days. (2) Usually newly formed protective adhesions will be torn. (3) Drains may be displaced. (4) Increased dissemination of pus, perhaps extending into the uterine cavity, may cause the fetus to become toxic.

The case is presented of a 21-year-old primipara who was admitted, at term but not in labor, complaining of constant pain in the lower abdomen of 12 hours' duration. Her temperature was 100 degrees F., pulse 104, respirations 20. Physical examination disclosed the entire abdomen to be very tender, with more marked tenderness in the right lower quadrant. There was no dilatation of the cervix. The white blood count was 18,200 with a 95 per cent polymorphonuclear count; hemoglobin was 48 per cent, red blood count, 2,800,000. Urinalysis was negative. The blood pressure was 110/78. A tentative diagnosis of acute appendicitis with possible rupture and generalized peritonitis was made. The patient was given 500 cc. of blood and operated upon immediately.

A low midline incision was made, and a gangrenous ruptured appendix was found. This was removed and the stump cauterized. A modified Porro section was performed in the following manner: The entire uterus was delivered out of the abdominal incision and the bladder peritoneal fold and bladder were stripped from the lower anterior uterine wall. Emphasis was placed upon the exact control of hemorrhage by dissecting free all ligaments before opening the vagina with adjacent connective tissue. The fascia was cut away from the cervix and the vaginal vault was then cut across transversely below the external os, removing the entire uterus. The baby was then delivered at another table by an assistant. No attempt was made to close the vaginal vault. Strips of gauze were placed at the opening of the vagina, and a drain was placed in the lower portion of the abdominal incision. Five grams of sulfadiazine powder were sprinkled

in the abdominal cavity and 100,000 units of penicillin were inserted into the lower pelvis.

Postoperatively, the patient was given blood, intramuscular and intravenous penicillin and nothing by mouth for 72 hours. Vitamins were given intramuscularly. Intravenous fluids containing sulfadiazine were given. At discharge on the twenty-first day, her blood count was 95 per cent hemoglobin; 5,100,000 red blood cells; 10,500 white blood cells. The patient was followed for one year and recovered uneventfully.

(Articles which set forth one or another side of a controversial issue are always of interest whether one agrees with the authors or not. Potter and Sadugor are not alone in their opinion because a number of other authors believe that radical intervention with the pregnancy is desirable whenever acute appendicitis develops in the last trimester. However, in an editorial note in the April, 1948 issue of the *Survey*, pp. 182-183, I ventured to set forth the other side of the question and firmly believe that uterine interference is unnecessary in such cases, especially with the modern availability of the sulfonamides and the antibiotics. In my opinion, the authors' 4 objections to the conservative management of these cases are more theoretical than real. Thus, Cosgrove has reported 18 cases of appendicitis in pregnancy in several of which labor followed very shortly after removal of a perforated, gangrenous appendix, but in spite of this, the postoperative courses were uneventful (*Am. J. Obst. & Gynec.* 34: 469, 1937). Nor, in similar cases, have we witnessed the much dreaded breakdown of protective adhesions with consequent peritonitis, which is so stressed by the proponents of radicalism.—Ed.)

PULMONARY EMBOLISM BY AMNIOTIC FLUID: A REPORT OF A FATAL CASE, TOGETHER WITH A REVIEW OF THE LITERATURE

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AND

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J. Obst. & Gynaec. Brit. Emp., 56: 46-53, February, 1949

The present case of pulmonary embolism by amniotic fluid is the sixteenth to be reported. The patient, a para i, aged 32 years, was first seen in the 32nd week of her second pregnancy. The findings on examination were essentially negative, except for a marked hydramnios and breech presentation. Spontaneous version had occurred by the 38th week. The patient was admitted to the hospital at term to await the onset of labor, with normal urine and blood pressure, vertex presentation with head floating, and marked hydramnios. Her condition

remained unchanged, and at 41½ weeks' gestation, medical induction was given, consisting of castor oil, an enema and 2 intramuscular injections of pituitrin (2.5 and 5 i.u.), the last at 6:30 P.M. At 6:45 P.M. the membranes ruptured. At 7:30 there were still no contractions and pituitrin (5 i.u.) was given. Five minutes later strong, frequent uterine contractions began. At this time the patient complained of "pins and needles" sensation in the arms and legs. At 7:40 the patient was cyanosed, with a weak, rapid pulse. Collapse followed, with marked dyspnea and coarse rales heard over both lungs. Despite the administration of oxygen and coramine, the patient died undelivered at 8:10 P.M., 35 minutes after the onset of symptoms.

Postmortem examination showed massive congestion and edema of the lungs. Particles of vernix were seen grossly in the blood contained in the heart. In the arterioles of the lungs, heart muscle and midbrain, and in the uterine venous sinuses, were blocks of typical squames. The uterus contained a large normal fetus. The membranes were ruptured over the cervix, and the presence of some unusually large veins in this region suggested a possible point of entry. On the other hand, although the membranes were intact in the region of the placenta and the latter was not detached, amniotic fluid was found to have tracked up between the membranes and uterine wall as far as the edge of the placenta. The amniotic fluid contained fresh blood and an abnormal amount of vernix.

Fourteen other recorded cases are reviewed, and the writers conclude that certain features combine to make this condition a clinical entity. The patient is usually a healthy multigravida with a large, maybe postmature, fetus. Labor is violent and the baby often stillborn. During labor, or shortly after delivery, there is a sudden onset of profound shock with cyanosis and dyspnea, terminating fatally in a few hours. At autopsy there is usually no obvious cause of death, but on microscopic examination of the lungs, emboli consisting of the particulate contents of the amniotic fluid, are found in the smaller pulmonary vessels.

The possibility of a sub-lethal type of embolism is discussed. Seltzer and Schuman (1947) recently described a case which they considered to be one of sub-lethal amniotic fluid embolism. Such a possibility raises the question of treatment. Steiner and Lushbaugh advocate large doses of morphine and atropine with oxygen inhalation, to lessen the reflex spasm in the lungs and cardiac depression. Treatment of shock with intravenous fluids is contraindicated because of the pulmonary edema. Postpartum hemorrhage must be anticipated and promptly dealt with if it occurs.

PATHOLOGY OF LABOR AND PUERPERIUM

LOCKED TWINS: REPORT OF 3 CASES

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J. Obst. & Gynaec. Brit. Emp., 56: 58-63, February, 1949

Three cases of locked twins are presented, together with a study of 28 other cases from the available literature. From an analysis of the total 31 cases, the writer postulates several etiologic factors.

The first of the present 3 cases was a gravida ii, aged 27 years, who was admitted in premature labor with some ankle edema, blood pressure 125/75, and a cloud of albumin in the urine. Six and one-half hours after admission the cervix was fully dilated; when labor had not advanced 2 hours later, it was decided to effect delivery. The head of the first twin was found in the pelvic cavity in right occipitoposterior position. The second twin was lying transversely with the head in the left iliac fossa, the back posterior, and the left arm prolapsed into the pelvis so that it lay beneath the posterior shoulder of the first twin. Manual rotation of the first twin to the anterior position was done, and the prolapsed arm pushed up. The trunk of the first twin was rotated and forceps delivery completed. Internal podalic version was then performed on the second twin, and breech extraction completed. The babies, both male, weighed 2,200 g. and 2,000 g., respectively. Mother and children were well on discharge.

The second patient, a 27-year-old primigravida, was referred to the hospital when 35 weeks pregnant for pre-eclampsia. After 9 days of treatment, her condition had not materially improved, and medical induction was given. Moderately good contractions began and the head of the first twin entered the pelvic brim. The pains ceased after completion of induction, and spontaneous labor began 14 days later. After 24 hours of labor, with no appreciable advance for 7 hours, delivery was attempted. A thin rim of cervix was still palpable and the head of the first twin was in right occipitoposterior position. The head of the second was entering the pelvic brim and was wedged above the head and beneath the shoulder of the leading twin. After the head of the second had been displaced upward, rotation and forceps delivery of the first twin was accomplished. The second twin was then delivered by forceps. The babies weighed 2,900 g. and 3,200 g., respectively, and both survived.

Case 3, a 21-year-old primigravida, was admitted in labor 2 weeks before term. Labor progressed normally; an hour after rupture of the membranes a foot was visible at the vulva. Delivery of the breech and trunk occurred without interference, but the shoulders were delivered with some difficulty. At this stage it was appreciated that the head had not entered the pelvis and that the neck

was considerably elongated. The head of the second fetus was then found low in the pelvis. An effort to displace the second head from the pelvis and permit delivery of the head of the first twin failed. Decapitation was performed on the first twin, which was already dead. The detached head was displaced from the pelvic brim, and the second fetus was delivered by forceps. The detached head was then delivered by grasping the neck stump with bullet forceps. The first twin, a male, weighed 2,700 g., and the second, a surviving girl, weighed 1,900 g. Mother and child were discharged well.

From an analysis of these and the other 28 recorded cases, it appears that deficiency of liquor amnii, either due to oligohydramnios or to early rupture the membranes, is frequently but not invariably present. Locking has occurred with large fetuses as well as with small ones, and a large pelvis is specifically mentioned only in occasional cases. However, one point observed which deserves comment is the preponderance of primigravidae. In the 31 cases there were only 6 mothers who had previously borne viable children. The remaining 25 patients were pregnant for the first time or had previously had abortions only. In this series, therefore, there were 25 first births, an incidence of 716 per 1,000. In a total of 953 twin births taken from several sources in the literature, there were 195 primigravidae, an incidence of 204 per 1,000. The difference appears to be statistically significant.

The author points out that uterine tone is greater in first than in subsequent labors, and the majority of cases were noted as having strong uterine contractions during labor. It may be deduced that strong contractions in a uterus whose basic tone is high are the effective factor in producing the sequence of collision-impaction-locking.

(Locked twins are pictured in almost all textbooks; and if you quiz a medical student about the complications of multiple pregnancy, he is almost certain to mention the difficulties which may ensue from locking of twins. Yet, in the 600 odd twin deliveries observed in our Clinic, not a single case has occurred, and in talking to obstetricians of large experience, I find that they likewise have not encountered any instance of this complication. As a consequence, I had even begun to wonder whether locking of twins ever did occur and was glad to be set right on this point by Lawrence's illuminating report. The fact, however, that he was able to collect only 31 cases from the literature is proof enough that this complication is the rarest of the rare.—Ed.)

DYSTOCIA AFTER AMPUTATION OF CERVIX

W. CALVERT

Brit. M. J., 1: 58, January 8, 1949

In 1938, a patient, then aged 40, was treated by anterior and posterior colporrhaphy and amputation of the cervix for procidentia. Because of the condition of the cervix, amputation was maximal. There had been 4 forceps deliveries, and subsequent pregnancy was not anticipated.

In 1944, the patient was admitted to the hospital, having been in labor for 2 days, and although the head was well down in the pelvis, her physician could distinguish no external os on vaginal examination. Examination was repeated in the hospital with the same findings. The head was separated from the examining finger by a thin sheet of muscle in which there seemed to be no aperture. Lower segment cesarean section was carried out immediately. Exploration of the lower pole of the uterus from above revealed no internal os, but a dimpling where the muscle seemed very thin. Vaginal examination after operation revealed no blood in the vagina, and the thin area of muscle was deliberately perforated so that the lochia could drain freely. The puerperium was satisfactory, but on vaginal examination on the 19th day, again no external os could be identified.

Obviously, some orifice must have survived the first operation for menstruation and conception to have taken place. The writer suggests that the aperture was very small, and that the swelling resulting from hypervascularity of pregnancy completed the closure.

(Postoperative cicatricial atresia of the cervix has long been recognized as a cause of dystocia. As early as 1883 Murphy (*Am. J. Obst.* 16: 28, 1883) reviewed 11 instances of this occurrence. Audebert (*Ann. de gynec. et d'obst.* 49: 20, 1898), Guibot (*Thesis, Paris*, 1900, No. 341, cited by Leonard) and LePage (*Bull. Med. Par.*, 947, 1903) reported difficult labors following trachelectomy, LePage's case necessitating Porro-cesarean section. In 1913 Leonard (*Surg., Gynec. and Obst.* 16: 390, 1913) tabulated the immediate and late results of 128 patients upon whom high amputation of the cervix had been done, and found that "fifty per cent of the pregnancies occurring after cervix amputation terminated prematurely while among the few who progressed to full term, even a larger proportion experienced difficulty and prolonged labor." A subsequent analysis by the same writer (*Surg., Gynec. and Obst.* 18: 35, 1914) of 39 cases of trachelorrhaphy indicated that following this operation labor was almost always normal. Rawls (*Am. J. Obst. & Gynec.* 3: 1, 1922) on the other hand, in an exhaustive study of the end-results of 211 cervical operations at the Woman's Hospital, New York, showed that in this series at least trachelorrhaphy rather than amputation predisposed to dystocia. Of his 32 trachelorrhaphy cases later becoming pregnant, 3 required cesarean section on account of cervical rigidity.

A good many years ago I had a case of spontaneous rupture of the uterus in labor following Sturmdorf tracheloplasty, which resembled the one reported above in that I was unable to locate any cervical opening (*Am. J. Obst. & Gynec.* 11: 500, 1926). Rupture of the uterus occurred after less than 11 hours of labor but the patient recovered after hysterectomy. Today, fortunately, cervical amputations, tracheloplasties and Sturmdorf operations, are not often performed on women in the childbearing period and, if so, are usually accompanied by sterilization.—Ed.)

OBSTRUCTED LABOUR DUE TO NAEGELE'S PELVIS:
REPORT OF A CASE

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J. Obst. & Gynaec. Brit. Emp., 56: 16-17, February, 1949

A case is reported of obstructed labor due to pelvic contraction of Naegele's type. This report is a reminder of the need to gauge carefully the capacity of the birth canal, even when routine pelvic measurements are normal.

A Chinese woman, aged 22, para ii, first attended the antenatal clinic at the 36th week of pregnancy. Her first labor, 18 months previously, had been difficult and terminated with forceps extraction of a dead baby with macerated scalp and fractured skull. Routine pelvic measurements were normal, but examination revealed scarring of the skin over the left sacro-iliac joint. At the age of 3, the patient had suffered from chronic inflammatory, probably tuberculous, disease of the sacro-iliac joint. Some pelvic asymmetry was noted with the patient in the scars are absent, so that the deformity would then be detected only by careful attention to the signs of asymmetry and by internal palpation. Furthermore, the authors state that the fact that the patient has delivered live children spontaneously in the past does not necessarily imply that she will do so in the future. 1 figure.

erect position, and there was a slight limping gait. An x-ray film illustrated the changes characteristic of an obliquely deformed pelvis of Naegele type.

Cesarean section was advised and scheduled for one week before the expected date of confinement. The patient failed to report to the hospital on this date, and 2 days later the hospital almoner found her at home, already in labor for some hours. She was persuaded to return to the hospital where a lower segment cesarean section was performed. By this time, she had been in labor 10 hours and was having severe uterine contractions. At operation, delivery of the head was not difficult, since it was still not engaged at the brim. The child weighed 3700 g., its head circumference was 35 cm., and both mother and child did well. Subsequent measurements of the mother's pelvis showed marked pelvic asymmetry.

The limp in such cases as this is not always obvious, and in congenital cases

(Bone tuberculosis is very common in north China and it is barely possible that Naegele pelvises are more frequent there than is realized. As the authors point out, these pelvises are not necessarily a deterrent to normal childbirth, especially if the baby is small, and it is easy to miss them if x-ray observations are not made.—Ed.)

Maternal Mortality Reports

(Secretaries of Maternal Mortality Committees are invited to submit selected cases of maternal deaths, with analyses appended, for publication in this section of the Survey. Cases should be chosen on the basis of educational value, not because of rarity. For obvious reasons complete anonymity will be maintained.)

Readers should note that the comment which follows each case history represents the opinion of the Committee concerned and does not necessarily reflect the attitude of the Editors.)

CASE NO. 78

The patient was a registered, white, private 26 year old primigravida with unknown serology, unmeasured pelvis, but positive Rh, whose last menstrual period is said to have begun December 2. On about February 19, when presumably at the end of the 11th week of gestation, she presented herself to her family physician for prenatal care. At this time she is said to have had a blood pressure of 118/64 and a pelvic mass which the physician thought was an enlarged uterus containing a pregnancy. No pelvic measurements were obtained, no serology determined, no blood counts obtained, and blood type and Rh were determined after hospitalization. Whether there had been any prior abnormal symptoms is not clear but there is the suggestion that there had been and that they had been handled via the telephone. However, it is certain that a week after this office visit she had abdominal pain and at least the major symptoms began at this time—(12 weeks' gestation). The following day she developed diarrhea and it appears that her physician considered this as an episode of gastrointestinal upset. It seems, from the available information, that she was seen for the second time at the physician's office on March 6 (13½ weeks' gestation) when she complained of having fainted. It appears that no importance was attached to this episode and she went home only to be hospitalized 2 days later.

She was admitted via ambulance to the hospital on March 8 with complaints of weakness, nausea with vomiting, fainting and abdominal cramps. According to the husband, these had been present for 2 weeks. The pulse rate was 100, respirations 47 per minute and temperature 101.4 on admission. She appeared pale and undernourished. The abdomen was distended, tense and the liver margin thought to extend a finger breadth below the right costal margin. It appears that no pelvic examination was ever done after the initial office visit and there is no mention of vaginal bleeding at any time. There was never a urinalysis. The admission blood count revealed the hemoglobin to be 26 per cent, red blood count 1.45 million, and white blood count 27,800 with 95 per cent polymorphonuclear leukocytes.

The initial treatment consisted of sedation and of intramuscular injection of liver extract. Just what this could do to the severe anemia is certainly not clear. These injections were continued daily and oral injection of iron, Folvoron, and a high protein diet were added. On the day after admission, as well as on the 4th and 8th hospital days, she was given a transfusion of approximately 500 cc. of fresh citrated blood. The second blood count was obtained on the 5th hospital day and revealed 50 per cent hemoglobin and 2.75 million red blood cells, which were the same on the subsequent days, i.e., 6th and 9th days in the hospital.

Abdominal pain was a major complaint throughout her hospital stay. The physician seems to have recognized the progressive anemia but didn't think of an extra-uterine pregnancy and held to a diagnosis of a dead fetus. One wonders how he could possibly account for the anemia in the absence of external bleeding. The patient's temperature fluctuated daily between normal and 101, and pulse remained between 110 and 120 per minute with respirations constant at about 30 per minute. The abdominal distension is said to have increased gradually but the physician interpreted this as gaseous (intestinal) in origin and on the day before exitus he began Wangenstein suction. Not a single blood pressure is recorded as having been obtained during the whole hospital stay.

On the morning of the 9th hospital day, after at least that many days of unwarranted procrastination, the nurse's notes record sudden abdominal pain, shock, increasing pallor, restlessness, cold clammy skin, anxiety and then stupor. The physician was not immediately available so the nursing staff called in 2 physicians who were near but the patient by this time was in extremis and no amount of heroic therapy could undo the professional idleness of the previous 9 or more days.

What is described as a postmortem examination was performed at a funeral home on an unstated date. It was limited to the abdomen. The whole report does not occupy a single page of writing. Its only value is that it contains such statements as: "the peritoneal cavity is filled with blood"; "the uterus is slightly enlarged and softer in consistency than usual"; "the left tube is dilated and has previously perforated," and "it is imbedded in a large mass of organized blood clot."

Cause of Death. Intra-abdominal hemorrhage following rupture of tubal pregnancy at 15 weeks' gestation.

Preventability of Death. Preventable.

Responsibility for Death. Physician.

CRITICISM

One cannot escape the criticism that this was a preventable death and that full responsibility must rest with the family physician, the only one who saw the case except in its terminus. What further signs or symptoms could he need to make him consider the possibility of an extrauterine pregnancy? Any consultant with a small bit of imagination would have immediately guessed the true nature of the disease. Adequate supportive therapy (transfusions) would have prolonged her life indefinitely. Even careful pelvic examination would have shown that this was not an intrauterine pregnancy. The physician's rationale in trying to explain the signs and symptoms in terms of a "dead fetus" is about as far-fetched as one could guess. These glaring errors of omission were preceded by lesser ones; the patient obviously had characteristic signs and/or symptoms for at least 2 days, if not even 2 weeks, prior to hospitalization.

CASE NO. 79

The patient was a 35 year old registered, private, colored para 4-0-1-3, with unknown Rh, unmeasured pelvis, but negative serology, whose last menstrual period is said to have begun August 10, making her estimated date of confinement May 17.

Her previous health is said to have been good with no serious illnesses. Her first pregnancy is said to have ended in early abortion. The next 4 were carried to term with easy deliveries conducted by a midwife. The last puerperium was associated with marked bleeding and this prompted her to seek medical care with the final pregnancy.

For the 6th and final pregnancy she presented for care on December 28, i.e., in the 20th week of gestation. Her blood pressure was 134/100, the pelvis is said to have been normal but no measurements are given to substantiate this, and the only laboratory work done was the blood Wassermann which was negative. A salt free diet was recommended and, in spite of the toxemia blood pressure reading, she was advised to return in a month. Instead, she came back in 5 weeks when the urine is said to have been negative; she had gained 2 pounds and her blood pressure was 140/90. Again she was advised to return in one month. She was, however, not seen again until hospitalization 7 weeks later.

On March 21, at 32 weeks' gestation according to the menstrual history, she fell into

labor and shortly thereafter a bloody show appeared. She had had some vaginal bleeding 2 days before but thought little of it as shown by the fact that she did not report it. En route to the hospital she began passing clots. Upon arrival her pulse rate was 120 per minute, blood pressure 110/70, her skin was clammy and she was perspiring profusely. Her uterus was tense and bleeding described as being "free" with the passage of some clots. Vaginal examination revealed a thin but firm cervix which was 2.5 cm. dilated with membranes unruptured and presenting pole unengaged. She was given morphine and then intravenous calcium, plasma (250 cc.) and 10 per cent glucose in saline (1000 cc.).

Two and one-half hours after hospitalization a fellow practitioner was called because the patient had shown no improvement. He confirmed the diagnosis of premature separation of the normally implanted placenta and recommended palliation inasmuch as the patient was then a poor operative risk for cesarean section which both the physician and the consultant would have preferred doing. They thought her condition too critical for even induction of labor by membrane rupture. The consultant advised plasma and blood. Apparently no prior arrangements for blood transfusion had been instituted. At long last, a transfusion of 500 cc. of whole blood was begun approximately 6 hours after admission. However, in the interim, she had received 2000 cc. of 10 per cent glucose in Ringer's solution in addition to a similar original amount. It appears that only one transfusion was anticipated. Certainly no more was given and she lived another 4 hours after the lone transfusion was started. This amount was obviously only a tiny fraction of that required to combat the shock and blood loss in this case. Moreover, by the time the transfusion was begun the patient was already showing advanced evidence of nearing the end of her capacity for neglect for at that time coramine and adrenalin were given followed an hour later by oxygen. She died undelivered 10 hours after hospitalization. There is no information to indicate that this patient's blood was typed for the Rh factor before she was transfused.

Cause of Death. Shock and hemorrhage due to premature separation of the normally implanted placenta at 32 weeks' gestation in a patient with arteriosclerotic toxemia.

Preventability of Death. Preventable.

Responsibility for Death. Original physician.

CRITICISM

Faulty care of this patient began with the very first prenatal visit. Patient study was essentially nonexistent. The chief criticism here is that she obviously had arteriosclerotic toxemia but was given no active therapy for it and was not instructed to return within a month. The same error was made at the only follow-up prenatal visit. Apparently nothing was done to check up on this patient when she did not return for prenatal care on schedule. After admission, the delay in instituting transfusion therapy was reprehensible. Certainly cesarean section was out of the question so long as shock and blood loss were not adequately controlled. However, membrane rupture upon admission might well have partially checked the continued blood loss. Obviously also, infusions of plasma should have been continued uninterruptedly until blood, in adequate amounts, was available. Too much dependency was placed upon glucose infusions which are known to be the poorest substitutes for blood loss and the poorest infusions for treatment of shock. The greatest errors in handling this case appear to have been in connection with the treatment of shock and blood loss, i.e., too little and too late.

CASE NO. 80

The patient was a 36 year old, registered, white, private primigravida with unknown serology, unknown Rh factor and unmeasured pelvis, whose last menstrual period began on September 26 to make the estimated date of confinement July 3. She presented herself for prenatal care on March 11, at the end of the 24th week of pregnancy. No blood pressure, weight or other specific data are recorded for this first prenatal visit. Follow-up prenatal visits were at 2-week intervals until gross pathology developed. These visits included the minimum requirements for adequate care. Weight gain was excessive, $7\frac{1}{2}$ pounds between the 28th and 30th weeks of pregnancy with no noted previous pathology except for edema of the feet for which "nutritive capsules" had been given. Blood pressure continued in the neighborhood of 130/80 from the onset of care. At the next visit there was no record of weight or urinalysis. At the 34th week there was hypertension of 140/88 with a trace of proteinuria, without excessive weight gain, for which magnesium sulfate was ordered. Two weeks later there was no weight obtained, blood pressure was 160/100 and there was a trace of proteinuria; "Nephretin" was ordered. After another week the blood pressure had climbed to 170/100, proteinuria is recorded as 2+ and ascorbic acid was ordered. A week later, the 37th week of gestation, there was no weight, blood pressure was 200/130 and there was a 4+ proteinuria. At long last the physician apparently began to realize that something was not just right so he sent her home to take castor oil for induction of labor. This failed and on the following day blood pressure was 220/140; proteinuria remained 4+ and she was not weighed but admitted to the hospital for induction of labor with intramuscular pitocin.

Pitocin in doses of 2 minims every 30 minutes for a total of 9 doses failed to induce labor. Apparently as a result of restricted activity but under no other specific toxemia regime, the blood pressure is said to have been lower but still elevated on the day after admission, and it was believed she was improving and could be carried on in pregnancy. There are few blood pressure recordings revealed after hospitalization. On the 4th hospital day, approximately $3\frac{1}{2}$ weeks before the estimated due date, an associate physician is said to have seen the patient in consultation and to have advised cesarean section, but there is no note to this effect by the consultant. However, cesarean section, elective classical, was done and the downhill skid was accelerated. Nitrous oxide and ether anesthetic was given by another family physician. Preoperative medication of demerol was given (10 minims prior to surgery). The patient's condition under anesthesia is said to have been fair with pulse rate 136 per minute, respirations 28 per minute and blood pressure 190/115. At the end of operation her condition is described as good with pulse rate 92 per minute but no blood pressure recording. In fact, the next blood pressure, 150/110, appears the following day. An unweighed living child which survived (estimated to weigh $6\frac{1}{2}$ pounds) was obtained.

The early postoperative course was complicated by bleeding from the abdominal wound for which the wound was reopened and packed with hemostatic gauze. Although the patient's condition upon hospitalization was not good, there was no laboratory work done until the 7th day, 2 days after operation. There was now 3+ proteinuria with urine loaded with pus. Hemoglobin was 48 per cent and red blood count 2.22 million. On this day a transfusion of 400 cc. of blood was given. It is said to have been compatible even for the Rh factor but this factor is unstated. The blood group was II (A). Two other donors were typed and crossmatched the following day but no further transfusion therapy was given though the patient managed to survive 8 days after the transfusion. The only other blood study was done 5 days before death revealing nonprotein nitrogen to be 40 mgm. per cent. Not many specific data on her subsequent course are revealed. Penicillin was, however, given in the early postoperative course. Glucose was given rather sparingly in unstated diluents. Duodenal suction was used as well as prostigmin. A hodge-podge of other therapy, including vitamin E and "Fleets," was given. There was oliguria from the time of delivery on until death with a maximum of 100 cc. of urine per day on the days in which it was recorded. Two days before death she is said to have "voided a large amount of bloody urine." On the day of death, the 14th in the hospital and the 8th after delivery, she developed some type

of convulsive seizures which, because of the time element, must be considered as uremic in type. Permission for postmortem examination was not requested because the physician in charge "was away at the time of death."

Cause of Death. Uremia with untreated severe preeclampsia and following delivery by cesarean section with postpartum abdominal hemorrhage at 37 weeks of gestation in an elderly primipara.

Preventability of Death. Preventable.

Responsibility for Death. Original physician.

CRITICISM

It is easy to see that this was a preventable death with physician care being directly responsible for this death. Care by a midwife could hardly have been worse. The first prenatal visit was little short of registration. The follow-up visits were well enough spaced and the routine check-ups generally complete. But the way in which this toxemia was allowed to develop without acceptable therapy for it, through all stages beginning with excessive weight gain and going on to severe and fulminating preeclampsia, is revealing and discouraging. The lassitude in the face of gradually rising blood pressure makes it appear that the physician was awaiting the onset of true eclampsia before being jolted into action. It seems remarkable that the patient did not accommodate him. His care of her after hospitalization is equally as negligent and faulty as prior to admission. The use of even the oxytocic fraction of pituitrin which is presumably free of pressor fraction, can hardly be considered acceptable therapy although labor and delivery were highly desirable. Fulminating pre-eclampsia should have demanded more drastic methods of induction either vaginally or abdominally. The belated cesarean section was not bad therapy except for the lack of hemostasis which represented careless or unskilled technic. Patient study throughout was reminiscent of bygone generations. Oliguria was known but little done to combat it. Medical recording was as inferior as patient study. Written consultations were as incriminating as the actual care given. Finally, the excuse for not having obtained an autopsy is not acceptable.

CASE NO. 81

This patient was a registered colored, private (originally), married 35 year old para 0-0-7-0 with a normal pelvis, negative serology and positive Rh, whose last menstrual period began on October 4, making her expected date of confinement July 11. She had never carried beyond the 4th month of pregnancy with any of her previous pregnancies, but neither the physician's nor the hospital's records contained any further information of the past obstetrical history. The family and menstrual histories are unimportant. She was known to have had some dyspnea ever since she was a child. In 1943 because of a nontoxic goiter she had had a thyroidectomy, after which she had some unspecified "difficulty" with her voice suggesting operative injury to the recurrent laryngeal nerve. Whether dyspnea persisted after the thyroidectomy is not mentioned. However, she did state that she had had slight swelling of the neck with each menstrual period and the swelling was more marked during pregnancy. Aside from the thyroid disease she mentioned no other serious illnesses.

She was first seen prenatally on February 25, i.e., with the pregnancy advanced into the 21st week. The physician who accepted her apparently did so at the specific request of a

white patient who was concerned about this negress' past obstetrical history, for he did not regularly accept colored patients. At this time no pathology of the heart or lungs was noted. The only notation relative to her thyroid was that she had a wheezing voice which was taken as a sequel of the operation 4 years before. Complete laboratory work showed normal findings except for a marked anemia (hemoglobin 55 per cent or 8.5 grams, and red blood count 2.75 million). In the absence of further mention of this or of therapy for it, it is assumed that the marked anemia was ignored. She was not seen again until 5 weeks later at which time there is no recorded weight. Her next visit was 3 days after the 2nd when she complained of dyspnea. Since there is no mention of chest findings, it is presumed that she was not examined. She was believed to have asthma and was given Benadryl. That this diagnosis was erroneous is proven by the fact that 4 days later she was admitted to the hospital with respiratory distress, cough, cold and dyspnea of 3 or 4 days' duration. It appears that there had been no contact with her since Benadryl had been prescribed.

When it became apparent that the laboratory work required would be expensive she was transferred to the charity service. It is assumed that admission was to the medical service. The emergency room examination revealed the blood pressure to be 100/50, pulse 130, respirations 22 and temperature 100.2, with bronchovesicular breath sounds in the mid-thorax on the right side posteriorly and laterally. This emergency room note claims that the present illness was of 10 days' duration and that Benadryl had produced little relief of her symptoms. The diagnosis then was asthma with mild pneumonitis or possibly pneumonia. Later in the day of admission her temperature rose to 102.0 F., with a pulse rate of 110 and respirations 36. X-ray of the chest showed infiltration of the lung in the right base as well as in the left cardio-phrenic area. There was an area of homogeneous density extending peripherally from the right paratracheal area which was continuous with the shadow of the aortic arch and associated with shift of the trachea to the left, from which an aortic aneurysm was suspected. Anemia was present (hemoglobin 61 per cent) with leucocytosis of 24,700 white blood cells. Besides the pregnancy, the admission diagnosis is given as (1) hyperthyroidism, (2) early bronchopneumonia and (3) laryngeal obstruction with edema due to an aortic aneurysm or to a substernal thyroid.

Therapy consisted of an initial dose of 100,000 units of penicillin followed by 50,000 units every 3 hours thereafter, plus phenobarbital, benadryl, and vitamins but no anemia therapy. Her temperature and respiratory rate fell but respirations became more labored and the obstruction appeared to be inspiratory in type. Although there is no recorded consultation, it is said that the surgical service pointed out that the obstruction was too low for tracheotomy to be helpful. It is said that an endotracheal tube was inserted but that the patient expired a few hours later. Since the patient died on the third hospital day, it is quite obvious that use of this life-saving measure was delayed until after the 11th hour. Apparently oxygen was not administered.

Permission for postmortem examination was granted and the autopsy was performed without examining the cranial contents. The report is one of the few scientifically performed and recorded ones which have been reviewed by this Committee. It is a distinct pleasure to read the report of another modern pathologist. The important findings at autopsy were: (1) bronchopneumonia in the right middle and lower lobes, (2) substernal thyroid, nodular colloid goiter in type with the gland 3 times as large as a normal thyroid and encroaching upon the right main bronchus causing (3) compression of that bronchus with partial atelectasis of the right upper lobe, (4) bilateral pulmonary edema, (5) purulent exudate in the right pleural cavity, and (6) pregnancy which had advanced to 26½ weeks. The uterus was not opened.

Cause of Death. Suffocation due to obstruction of a main bronchus by a substernal colloid goiter and to pneumonia with early empyema and pulmonary edema at 26½ weeks' gestation.

Preventability of Death. Preventable.

Responsibility for Death. Physicians, especially original physician.

CRITICISM

It seems to the Committee that this is very definitely a maternal death. Exitus in this case was due to suffocation as the result of obstruction of a main bronchus by a substernal colloid goiter and subsequent pneumonia. It is well known that thyroid tissue has a tendency to enlarge in pregnancy. In this specific case, moreover, it may be noted that the patient herself stated that she had a slight swelling of the neck with each menstrual period and that the swelling became still more marked during pregnancy. It is hence the Committee's feeling that the changes wrought by pregnancy on this patient's thyroid gland were the determining cause in her death and that she would in all probability not have died had not it been for the state of pregnancy.

The available data strongly suggest that this was a preventable death and that every physician who cared for her could have done something to prevent this unnecessary fatality. The original physician obtained the history of longstanding dyspnea. Instead of investigating this, he concluded that the wheezing voice resulted from injury to a recurrent laryngeal nerve. Consultation from a laryngologist with examination of the vocal cords would have very quickly proven this assumption false and should have led to bronchoscopy. This was at a time when the patient was in reasonably good condition and could have withstood chest surgery. Failure to treat the patient's anemia assumes lesser importance. His second chance came a few weeks later when the respiratory infection began. The erroneous diagnosis of asthma may be understood but failure to follow the patient's course until gravely ill is not excusable. The obstetrician should have recognized the symptoms requiring the services of a laryngologist and/or internist. The belated hospitalization was still not too late to do something more energetic to treat the obstructed upper respiratory passage. For example, why was oxygen never employed and why was endotracheal tube withheld until the end was in sight? The erroneous diagnosis of aortic aneurysm with inoperability at the moment was no excuse for not employing every available medical and minor surgical means until the patient was over the acute state of infection. Failure to treat, again, the marked anemia in the hospital is of minor importance. The excellence of the autopsy should be commended.

BOOK REVIEW

FUNDAMENTALS OF HUMAN REPRODUCTION. By Edith L. Potter, M.D., New York, McGraw-Hill Book Company, Inc., 1948, xii, 231 pp.

Dr. Potter has attempted with a considerable measure of success to present a simplified account of human reproduction, including the elements of genetics, of cycle physiology, and of embryology. She has gathered her materials with care from the best secondary sources, and has put them together into a book that is on the whole clear and well balanced. There is a profusion of black-and-white diagrams and a series of good photographs of the fetus and its membranes, from the author's own collection. Although the book is intended primarily for pupil nurses, college teachers of biology will no doubt put it on their lists for collateral reading. The publisher's blurb suggests that medical students also will find the book of great value as a synopsis of the material found in comprehensive works, but at this level the dangers of over-simplification become serious. As in many such attempts at semi-popularization of scientific subjects, there are lapses from reality resulting from over-diagramming in text and figures, and from the fact that so wide-ranging a book must often use material not directly familiar to the author. Some of these are trivial, others will blur the reader's comprehension. A few must be pointed out here, to illustrate the difficulties that have faced the author and to warn that advanced readers must go to higher sources if they want information that is accurate in a detailed way. The description of the menstrual cycle, for example, does not include anovulatory menstruation. This is admittedly a hard topic to simplify, but it is an essential part of the physiological thinking that underlies the clinical study of human sterility. A paragraph at the bottom of p. 63 suggests misleadingly that not all the estrogen produced by the ovary is transported by the blood-stream, i.e. that some of it reaches the uterus in another way, presumably by direct diffusion in the reproductive tract. The statement that the corpus luteum maintains "some activity" until the end of pregnancy is very dubious. The account of multiple births explains single-ovum twinning by assumed duplication of the inner cell mass of the blastocyst, ignoring the possibility of the formation of two or more embryos upon the embryonic disk developed as usual from a single inner cell mass. The scanty available evidence from mammals and man indicates that this latter type of polyembryony, occurring relatively late in development, is, to say the least, more common than the other possible modes. Future Dafoes who do not know this will not be fully equipped to analyze the cases of multiple birth they may chance to observe. A diagram of the placental circulation of fraternal twins with fused placentas (fig. 36,B) shows a wide-open communicating blood circulation, something that is probably not usual in humans. This might well confuse students who know the story of free-martins in cattle.

Some of the diagrams are very helpful in explaining the elementary processes of embryonic development, as for example figure 42, which illustrates the relation of the incipient embryo to the membranes in an exceptionally clear way. Others suffer from over-simplification and lack of realism. There are students who will

assume from figure 26 that human ova are as big as marbles and that the uterus and fallopian tube have wide-open lumina of approximately the same size. A little diagram at the head of a chapter on the heart and blood vessels (p. 156), which shows four arterial vessels in the umbilical cord, will perplex many readers.

In spite of such evidences as these that the author and illustrator are sometimes working without first-hand experience of the topics discussed, the book makes a conscientious effort to explain the complex subject and is the best available account of human reproduction for nurses and others who must study the subject with little opportunity for laboratory investigation. There is a bibliography listing good text-books and popular works on the various branches of biology touched on in the book. A list of relevant motion picture films will be appreciated by teachers.

GEORGE W. CORNER

BOOK REVIEW

FUNDAMENTALS OF HUMAN REPRODUCTION. By Edith L. Potter, M.D., New York, McGraw-Hill Book Company, Inc., 1948, xii, 231 pp.

Dr. Potter has attempted with a considerable measure of success to present a simplified account of human reproduction, including the elements of genetics, of cycle physiology, and of embryology. She has gathered her materials with care from the best secondary sources, and has put them together into a book that is on the whole clear and well balanced. There is a profusion of black-and-white diagrams and a series of good photographs of the fetus and its membranes, from the author's own collection. Although the book is intended primarily for pupil nurses, college teachers of biology will no doubt put it on their lists for collateral reading. The publisher's blurb suggests that medical students also will find the book of great value as a synopsis of the material found in comprehensive works, but at this level the dangers of over-simplification become serious. As in many such attempts at semi-popularization of scientific subjects, there are lapses from reality resulting from over-diagramming in text and figures, and from the fact that so wide-ranging a book must often use material not directly familiar to the author. Some of these are trivial, others will blur the reader's comprehension. A few must be pointed out here, to illustrate the difficulties that have faced the author and to warn that advanced readers must go to higher sources if they want information that is accurate in a detailed way. The description of the menstrual cycle, for example, does not include anovulatory menstruation. This is admittedly a hard topic to simplify, but it is an essential part of the physiological thinking that underlies the clinical study of human sterility. A paragraph at the bottom of p. 63 suggests misleadingly that not all the estrogen produced by the ovary is transported by the blood-stream, i.e. that some of it reaches the uterus in another way, presumably by direct diffusion in the reproductive tract. The statement that the corpus luteum maintains "some activity" until the end of pregnancy is very dubious. The account of multiple births explains single-ovum twinning by assumed duplication of the inner cell mass of the blastocyst, ignoring the possibility of the formation of two or more embryos upon the embryonic disk developed as usual from a single inner cell mass. The scanty available evidence from mammals and man indicates that this latter type of polyembryony, occurring relatively late in development, is, to say the least, more common than the other possible modes. Future Dafoes who do not know this will not be fully equipped to analyze the cases of multiple birth they may chance to observe. A diagram of the placental circulation of fraternal twins with fused placentas (fig. 36,B) shows a wide-open communicating blood circulation, something that is probably not usual in humans. This might well confuse students who know the story of free-martins in cattle.

Some of the diagrams are very helpful in explaining the elementary processes of embryonic development, as for example figure 42, which illustrates the relation of the incipient embryo to the membranes in an exceptionally clear way. Others suffer from over-simplification and lack of realism. There are students who will

assume from figure 26 that human ova are as big as marbles and that the uterus and fallopian tube have wide-open lumina of approximately the same size. A little diagram at the head of a chapter on the heart and blood vessels (p. 156), which shows four arterial vessels in the umbilical cord, will perplex many readers.

In spite of such evidences as these that the author and illustrator are sometimes working without first-hand experience of the topics discussed, the book makes a conscientious effort to explain the complex subject and is the best available account of human reproduction for nurses and others who must study the subject with little opportunity for laboratory investigation. There is a bibliography listing good text-books and popular works on the various branches of biology touched on in the book. A list of relevant motion picture films will be appreciated by teachers.

GEORGE W. CORNER

Gynecology

ENDOCRINOLOGY

ON THE MECHANISM OF THE ACTION OF OESTROGENIC HORMONE PREPARATIONS IN OVARIAN INSUFFICIENCY

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Acta endocrinol., 1: 171-188, 1948

The writers define stimulation and substitution therapy with hormones. We are dealing with stimulation therapy when by means of hormonal treatment we set in action a physiological mechanism which at the moment is at rest but otherwise functions spontaneously, and when this mechanism at least has a tendency to continue to function after the treatment. We speak of substitution therapy, however, when the hormone only acts directly on the receptor organ in a certain regular proportion to the administered amount of the hormonal substance and only for so long as it is being introduced into the organism or perhaps furnished from a depot if dealing with injection treatment. Obviously, it is desirable to use methods in hormonal treatment which have the character of stimulation therapy if conditions are present at all to permit it.

Rydberg, et al., 1939, 1943, and Westman, 1941, have found it possible by hormonal treatment to achieve an effect corresponding to what is meant by stimulation therapy when treating cases of ovarian insufficiency with gonadotrophic hormones. In the present paper, the writers examine the activity of the estrogens in their clinical application from the point of view of stimulation or substitution therapy in cases where a substitution therapy is conceivable and not a priori out of the question. Kaufmann (1935, 1937) and Westman (1941) have treated amenorrheic patients with estrogens, and their results tend to support the idea that such treatment is more than pure substitution therapy. Westman produced regularly recurring cyclic bleedings in 30 out of 64 cases of secondary amenorrhea.

Synthetic estrogenic preparations present new possibilities for studying the reactions of the ovary. "Sexadien" or di(p-oxyphenyl)-hexadien was used in the present study, and when given by mouth it seems to pass the liver without being broken down, disappearing from the organism within 24 or at the most 48 hours. This means that it was possible to conduct hormone analyses a few days after treatment had been terminated, and if a distinct increase in estrogenic excretion were found, as compared to that before treatment, it could be concluded that the increase was due to a hormonal source in the organism itself—that the ovary most likely had been stimulated to produce estrogen.

Forty-nine cases of amenorrhea were treated with Sexadien, with each patient receiving a total of about 100 mg. orally. In 18 cases estrogen output was determined before and after treatment. In all cases but one the hormonal analysis after treatment was made so late that the Sexadien given must have disappeared from the urine. The results from these analyses were:

I. Abnormally low values before treatment and unchanged low values after the treatment in 8 cases.

II. Abnormally low values before treatment and a slight but hardly significant rise of the output after treatment in 3 cases.

III. Low values before treatment and lower values after treatment in 2 cases.

IV. Abnormally low values before treatment and definite rise of output after treatment in 5 cases.

In 4 cases pregnancy occurred in close connection to the treatment. It is concluded that this activation occurs by way of the pituitary gland. Eighty endometrial biopsies were obtained from the 49 patients, with 10 showing secretory changes which would have been impossible for Sexadien alone to effect.

These experiences are strong supports for the conception of the treatment with estrogenic preparations being sometimes more than pure substitution therapy. The chances for practical results in the treatment of ovarian dysfunctional conditions in younger women are, however, apparently much better when gonadotrophins are given in rational dosage. 6 figures.

(The gist of this paper is that the use of estrogens in cases of ovarian insufficiency, often derided as purely substitutional, may actually serve a stimulating as well as a substitutional purpose, in the sense in which these two terms are defined by the authors. This theory is apparently supported by some of the hormone excretion studies made by them after the administration of an oral estrogen. On purely clinical grounds, many have felt that this may at times be true, since in at least a small proportion of cases this form of therapy is later followed by the occurrence of spontaneously recurring menstruation. However, the incidence of good results attributed by the authors to Westman (30 of 64 cases of secondary amenorrhea) is higher than most gynecologists would claim, and it is difficult to be sure how many such sequences can be attributed to the treatment, as even without treatment menstruation is not infrequently reestablished in amenorrhea of the secondary type.—Ed.)

PROGESTERONE PRIVATION TEST OR MEDICAL CURETTAGE. ITS APPLICABILITY IN THE DIAGNOSIS AND CLASSIFICATION OF AMENORRHEAS

F. A. DE LA BALZE

Sem. Med. (La Semana Medica) 55: 953, 1948

The progesterone privation test was utilized in 56 cases of amenorrhea. This test is based upon Zondek's investigations, which consist of the injection of 10 mg. of progesterone for 5 consecutive days, leading to the appearance of menstrual bleeding. The latter is not observed, however, when there is extreme estro-

genic deficiency present. The following method was utilized: intramuscular injection of 5 mg. of progesterone for 5 consecutive days, being the test considered positive when bleeding appears before the 5th day following the last injection, and negative when no bleeding is revealed within that stated period. All cases were controlled with vaginal smears. There were 30 negative results: in 20 there was lack or diminution of estrogenic activity, and in 10 estrogenic activity proved to be normal. Within the latter there were cases of amenorrhea due to pregnancy, atrophy or lack of responsiveness of the endometrium, and in 3 hemorrhage occurred following the 5-day period.

A positive test indicates a normal functioning endometrium; that there are sufficient circulating estrogens to stimulate the endometrium.

According to the author's opinion, bleeding following administration of progesterone, is due either to vascular changes or to alterations in the blood level of estrogenic hormone, since no progestational changes are observed in the endometrium.

The progesterone privation test is considered to be of great help in the hormonal diagnosis of amenorrheas, especially in view of its simplicity and rapidity.

(The progesterone method described by the author has, since the publication of Zondek's original paper on the subject, been employed by a good many American gynecologists in the management of amenorrhea. As the author states, the occurrence of bleeding after the last progesterone injection presupposes the presence of at least some estrogen in the patient's blood, as is likely to be the case in most instances, especially in the amenorrheas of secondary type. When bleeding fails to appear after the progesterone, repetition of the progesterone must be preceded by a modest priming of the endometrium with estrogen.

The same general principle has been applied as a means of cyclic therapy in functional bleeding, the progesterone privation effect produced on the endometrium being picturesquely spoken of as "medical curettage." Whether the results yielded by progesterone are any better or as good as those of the now more popular plan of controlling such bleeding with estrogen alone, I personally doubt, although it may be admitted that the good results of the latter are effected through simple hemostatic control and not by cure of the underlying pituitary dysfunction. I believe that pretty much the same criticism can be made of other available endocrine treatments of functional bleeding, including the use of progesterone. —Ed.)

INDICATIONS FOR HORMONAL PELLETS IN THE THERAPY OF ENDOCRINE AND GYNECIC DISORDERS

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Am. J. Obst. & Gynec., 57: 294-301 (Feb.) 1949

The implantation of hard compressed pellets of crystalline steroids results in the slow, more physiologic absorption of the hormone than that observed after parenteral administration. Economy and avoidance of repeated hypodermic punctures also recommend this technique.

With the use of the Kearns Pellet Injector, pellet implantation is a simple office procedure. A detailed description of its use is presented.

Some of the indications and contraindications are listed. A number of typical case reports, in which pellet implantation was of definite benefit to the patient, are cited. It appears that the pellet method of hormonal administration has more nearly approached the endogenous rate of hormonal secretion.

Testosterone and desoxycorticosterone acetate are now commercially available, and it is hoped that estradiol and progesterone pellets will soon be available. 6 figures.

(While the study of the effects of the implantation of hormonal pellets is of scientific interest, I confess that I have never been able to work up much interest in this particular route of therapy in the field of gynecological therapy. During recent years, for example, there have been many publications extolling the virtues of implanting pellets of estrogen in the treatment of menopausal symptoms. The chief advantage claimed for the method has been that it keeps up a fairly steady supply of estrogen for a considerable time. But this is the very thing we should avoid in the menopausal woman, in whom estrogens are indicated only when and if vasomotor symptoms are sufficiently troublesome, and never continuously. The chief hazards of continuous, so-called maintenance therapy are the induction of postmenopausal bleeding and the prolongation or retardation of the endocrine readjustment which the menopause inevitably entails. Modern methods of oral estrogenic therapy possess far greater flexibility than can be obtained from pellet implantation, and they involve no inconvenience to the patient. The hypodermic route appears to be definitely on the way out, although such "shot" therapy is still unfortunately used by a good many practitioners. The above comment applies only to pellet implantation as applied to the treatment of menopausal symptoms, and would not necessarily hold good for the administration of certain other hormones, such as desoxycorticosterone or testosterone, with which at times continuous therapy might be a desideratum.—Ed.)

MODE OF ACTION OF ESTRADIOL BENZOATE IN OIL SOLUTION AND OF AQUEOUS SUSPENSION OF CRYSTALS (THEELIN) IN THE CASTRATED FEMALE

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Obst. y Ginec. Latino-Amer. 6: 223, 1948

A comparative study is made by administering estradiol benzoate in oil solution and aqueous suspension of crystals (Theelin) in 5 women—4 castrated and 1 beyond menopause for many years with definite signs of lack of hormonal activity. The author arrives at the following conclusions: 1) It is necessary to give 1 mg. of estradiol benzoate in oil solution in order to produce definite changes in the vaginal epithelium of castrated women. 2) Following a single injection, estrogenic activity controlled by serial vaginal smears reveals a curve which begins on the 3rd day, gradually increases up to the 9th, when regression takes place until the 12th day. 3) In the woman, likewise in rodents, a latent

period is observed following administration of single doses, which, as a matter of fact, does not vary fundamentally by applying doses of 1 or 2 mg. 4) Estrogenic reaction curve in women, as measured by the changes in the vaginal contents, is approximately the same as the one observed in the uterus of rodents. 5) Examination of the vaginal contents and the measure of the vaginal reaction following a single injection of estrogens may prove to be of clinical value in order to determine and utilize the minimal doses necessary for the individual case. 6) There is no substantial difference in the changes produced in the vaginal mucous membrane by applying single injections of either estradiol benzoate or aqueous suspension of crystals (Theelin) in the dosage already mentioned (1 and 2 mg.).

THE MENSTRUAL CYCLE

THE PROPER MANAGEMENT OF FUNCTIONAL MENSTRUAL DISORDERS

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M. Clin. North America 32: 1509-1522, November, 1948

In treating menstrual disorders the physician must be cognizant of the fact that such disturbances are only symptoms of some underlying factor. In some instances, symptomatic therapy may be urgent; in others, as in some cases of amenorrhea, no therapy at all may be indicated. The maintenance of normal fertility and endocrine evaluation of the etiological factors and the age, physical and psychic condition of the woman are important considerations in the selection of a method of treatment.

In an evaluation of etiologic factors, it must be remembered that the maturation and release of a fertilizable ovum is the acme of perfection in the pituitary and ovarian function. Thus, any disturbance in this area or in the uterine physiology may result in a disordered menstrual cycle.

The presence of a malignant or other serious lesion must be ruled out by appropriate diagnostic measures. Frequently the correction of abnormalities will yield gratifying results in the treatment of functional menstrual disorders.

The sex-endocrine cycle is very labile and reacts easily to factors in the soma or psyche. Menstrual disorder may be one of the earliest manifestations of such diverse conditions as tuberculosis, leukemia or anorexia nervosa. General or systemic factors may affect either the ovarian or the pituitary function. It is often difficult to tell which elements of the pituitary-ovarian mechanism is affected without gonadotrophic assays.

True diseases of the pituitary or ovary are relatively rare. However, pituitary tumors, functioning tumors of the ovary and non-neoplastic cystic diseases of the ovary usually result in the menstrual disorder. Marked disturbances of the thyroid influence the menstrual cycle through the effect on the pituitary. Adrenal cortical dysfunctions result in an estrogen-androgen imbalance.

The importance of nutritional and metabolic disturbances in menstrual disorders is being studied. Amenorrhea in malnourished groups and the role of vitamin B complex in the inactivation of estrogen are indicative of the importance of such factors.

General hygienic measures are important in the therapeutic approach. But, in addition, the physician must determine whether or not more specific treatment is required. The importance of psychotherapy, even on a very simple level, must not be overlooked.

Thyroid extracts have been the sheet anchor in the management of menstrual

disorders for a long time; however, the author warns against its use on a trial basis. Vitamin therapy, particularly Vitamin E, has been used with success. The author feels that the use of oxytocics for the control of excessive bleeding is questionable.

The gonadotrophic and gonadal hormones are the most specific medications employed. But hormonal therapy must be administered with extreme caution. Best results with follicle-stimulating gonadotrophic substance are obtained in cases of excessive bleeding. They should be administered in a cyclic fashion. Chorionic gonadotrophin and prolactin are of some value in the treatment of menorrhagia. Estrogens are rational therapy for a primary ovarian dysfunction and can be useful in the menopausal syndrome. Progesterone with its regulating effect on the pituitary-ovarian cycle is becoming increasingly valuable.

In the use of irradiation therapy or surgery a critical evaluation of the effect on fertility and ovarian function is a prime consideration.

(A comprehensive and sound survey of a large field. Gynecologists differ, of course; in their attitudes on certain subjects. For example, I question whether most of them would agree with the author's statement that "best results with follicle-stimulating gonadotrophic substance are obtained in cases of excessive bleeding," and for that matter, a good many will question whether this hormonal preparation has achieved much of a therapeutic niche for itself in the management of any of the functional disorders. Again, as one of the early advocates of the use of the chorionic gonadotrophic hormone in the treatment of functional bleeding, I feel justified in suggesting that other hormonal plans developed since 1932, when our own studies were published, are much more likely to bring about control of the excessive bleeding. As for prolactin, I am even more skeptical. These few comments illustrate what I said as to individual variations in viewpoint and experience.—Ed.)

DANGERS IN THE MANAGEMENT OF THE CLIMACTERIC

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M. Clin. North America 32: 1523-1532, November, 1948

The climacteric is a normal, orderly and progressive event and not a pathological process. The failure of ovarian function produces physiological changes which may manifest themselves in a variety of symptoms. Cessation of menstruation, hot flushes accompanied by perspiration and weakness, and retrogressive changes in the uterus, ovaries and external genitalia are characteristic.

An investigation by the Medical Women's Federation of England of the climacteric history of 1000 women revealed that 15.8 per cent of the women had no menopausal symptoms. The most frequent symptom was hot flushes. Of the 1000 women, 89.7 per cent carried on their daily routine without interruption. A patient with a normal menstrual history tends to have few symptoms at menopause.

Any therapy used at this stage must be devoted to easing the patient through this period. Many women do not require any specific therapy. A careful history and physical examination and a meticulous search for malignant disease must be the first steps in the management of the climacteric.

The patient must be aided to become adjusted to her new state. An attempt must be made to eliminate from her mind misconceptions about the abnormality of this time. Satisfactory talks concerning her attitudes and way of life are more important than hormonal therapy. Mild sedatives may be prescribed to control the intensity of the symptoms. Only when all other measures have failed, is the giving of estrogen justified. In prescribing estrogen the smallest possible dose should be given, with frequent rest periods in therapy.

Too often when a patient in the fifth decade of life presents herself to the physician, she is told that her symptoms are due to the menopause and estrogens are prescribed without even an examination. The dangers in such a plan are numerous. The problem of irregular bleeding may be functional or organic in origin. Indiscriminate use of endocrine products for the control of irregular bleeding has led to delay in the diagnosis of uterine cancer. An abstract of a case in which the patient was treated for bleeding by endocrine injections for one year before the discovery of a carcinoma of the cervix is presented.

Often definite organic lesions of other systems of the body may be overlooked by attributing the symptoms to the climacteric. A case of a 41-year-old patient who was treated for vertigo and headaches by hormonal injections for almost a year before a diagnosis of an aneurysm of the cerebral artery was made, is discussed.

Gastrointestinal disturbances are often passed over in the taking of a climacteric history. There seems to be no evidence that arterial hypertension is related to the menopause. Endometriosis may be reactivated by the excessive use of estrogens. Estrogens are often needlessly administered to patients in need of psychiatric care.

The ill-advised administration of estrogen can produce hyperplasia of the endometrium. That this may also predispose to endometrial carcinoma is not unreasonable. There is increasing evidence of the relationship between uterine malignancy and prolonged estrogen therapy.

Contraindications to estrogen therapy are the previous use of x-ray or radium therapy for abnormal bleeding, history of pelvic malignancy, family history of malignancy or previous benign neoplasms. In short, estrogens can be of positive value in only a small group of carefully selected patients.

(This is a very sensible review, bringing out many points which have been stressed time and time again, but which are still widely disregarded by the general practitioners who treat such a large proportion of menopausal women. The author's statement that "many women do not require specific (i.e. estrogenic) therapy could be strengthened by insisting that only a small fraction need estrogens. Continuous administration of so-called maintenance doses is a wrong and pernicious custom. Estrogens have a definite place in the treatment of genuinely menopausal symptoms, especially the flushes and sweats, but they should be used only intermittently, when and if these vasomotor symptoms are sufficiently troublesome to constitute a real problem. The author might well have emphasized that the oral

route is always to be preferred to the hypodermic, to avoid the development of "shot" addiction. Finally, as the author intimates, the physician can earn his fees far more honestly and with greater benefit to the patient, by simple instructional and reassuring talks than he can by reaching for the hypodermic whenever a woman over 40 complains of all sorts of functional nervous symptoms, with usually none of the genuine hormone-withdrawal manifestations, as represented by flushes and sweats.—Ed.)

NEWER CONCEPTS OF MENSTRUATION

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Am. J. Obst. & Gynec., 56: 1037-1047, December, 1948

An explanation of cyclic uterine bleeding as a consequence of alterations of the coiled arterioles of the endometrium has gained widespread acceptance. However, the most recent laboratory findings as well as many familiar clinical observations require a return to a more general physiologic concept of menstruation as a result of withdrawal of metabolic support of the endometrium.

The cyclic changes of the vasculature of the endometrium are described. Markee, studying changes as they take place in endometrium transplanted to the anterior chamber of a rhesus monkey's eye, observed that the bulk of endometrial bleeding is arteriolar in origin and that, therefore, the coiled arterioles control the amount and rate of menstrual hemorrhage. Various vascular hypotheses are based primarily on these observations. These concepts assume that continued growth of a complex arteriole is a necessary precursor of menstruation.

One objection cited by the author against the hypothesis of a vascular mechanism for the initiation of menstruation is the amenorrhea of early pregnancy. It is reasonable to assume that the coiled arterioles in the relatively vast area of endometrium removed from the site of implantation differentiate to the same extent as in the nonpregnant uterus, at least in the 14 days following ovulation.

Another objection to the vascular explanation is the repeated observation that the coiled arterioles found in the presence of ovulatory menstruation differ considerably from those seen in anovulatory bleeding. Despite this fact, the clinically observed bleeding is identical in the two conditions. The author says that it must be remembered that bleeding can and does occur from an endometrium with a much simpler arteriolar bed, such as following oophorectomy or spinal cord transection done at the midinterval, or in cases of endometrial hyperplasia. Cyclic uterine bleeding of microscopic proportions occurs in the New World monkeys in which there are no coiled arterioles but, instead, a very simple system of small arterioles running through the endometrium almost without contortion.

These observations indicate that the explanation of menstruation based on

the vascular theory fails to account for much known about menstruation. Before a vascular explanation is abandoned, however, more information is needed concerning the contraction cones described by Daron.

Recently, Phelps, in studying the factor of previous estrogen treatment in the production of menstrual disorders in the rhesus monkey, found that "the influence of a single course of stimulation by ovarian hormones is not limited to the cycle which that course of stimulation represents. Its influence extends through at least one subsequent cycle and probably through more than one."

It is evident from this, the writer points out, that to function normally the epithelium, stroma and blood vessels must develop simultaneously to the same level of functional capacity. At present, it can be suggested that certain kinds of incoordinate growth of these three elements may be related to certain types of functional abnormality. Before a therapeutic regime for correction of infertility on the basis of menstrual abnormalities can be called a success, all three elements must have returned to normal. In this case, the endometrial biopsy should prove to be of increasing value as an index of therapy. 13 figures.

(The anatomical studies of Daron with his demonstration of the spiral or coiled arteriolar apparatus of the endometrium, followed by the important studies of Markee upon the behavior of these spiral vessels throughout the cycle, opened up a new chapter on the physiology of menstruation, although gaps have remained in our knowledge concerning the exact nature of the liaison between the spiral arterioles and the hormones. The objection offered by Kaiser to the hypothesis of a vascular mechanism for menstruation, on the grounds that the differentiation of a similar vascular apparatus in pregnancy is not associated with menstruation, does not seem to me a valid one. It is true that the spiral arterioles are highly developed in the early stages of pregnancy, but the endocrine set-up is quite different, in that the endocrine level remains high, in contrast with the periodic hormone drops in the menstruating woman. This indicates what I mean about the need for more knowledge of the relation of the hormones to the vascular apparatus. In spite of Kaiser's own investigations, there is also much need for elucidation of the differences in the vascular response in anovulatory as contrasted with ovulatory cycles.

Another confusing observation of recent years has been that there are no coiled arterioles at all found in the endometria of certain New World monkeys in which cyclic bleeding nevertheless occurs, though in only microscopic amounts. One must almost assume that there is in such animals an intrinsic hemorrhagic capacity in the endometrium itself, though this is of course anything but a scientific conclusion.—Ed.)

METRRORRHAGIA OF PUBERTY DUE TO LATE CONGENITAL SYPHILIS. CLINICAL CASE REPORT

U. M. PACHECO

Bol. de la Soc. Chilena de Obst. y Ginec. 13: 90, 1948

A 14-year-old female presented profuse metrorrhagia for 2 months at the onset of her first menstrual period. Pelvic examination was negative. History revealed pre-existing signs of syphilis, which was confirmed by the specific serological

tests. Hematogenic tests for blood dyscrasias were negative. Intense anti-syphilitic treatment was promptly instituted and genital bleeding subsided soon afterward. The patient was seen 3 years later presenting a normal menstrual history.

(I would be inclined to think that the bleeding in this case was of the common anovulatory functional type occurring in a patient who happened to be syphilitic, and in whom, as is so often the case, menstruation soon became normal through the establishment of ovulation. In other words, I believe that to give the credit to the antisyphilitic treatment is an instance of post hoc propter hoc reasoning. This statement seems justified when we consider the innumerable non-syphilitic functional bleeding patients who soon re-adjust themselves menstrually, and when we consider the complete lack of evidence to link up syphilis with this form of puberal hemorrhage, and for that matter, our ignorance of the whole subject of syphilis as it involves the female genital organs. For a discussion of this point, see comment on paper by Rudge and Delascio in this issue of the Survey.—Ed.)

VULVA AND VAGINA

VAGINAL CYTOLOGY OF POSTMENOPAUSAL WOMEN

STUDY I. CYTOLOGIC VARIATIONS IN VAGINAL SMEARS

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Duke University School of Medicine and Hospital, Durham, North Carolina

South. M. J., 41: 861-869, October, 1948

The patients in this study were divided into 2 groups: patients with and patients without malignancy. There were 70 patients in the former group and 257 in the latter. The vaginal smears were divided into subtypes according to the classification of Papanicolaou and Traut. Subtypes supplementing this classification were created in order to define and describe more accurately the postmenopausal vaginal cytology from the point of view of morphology. The subtypes which have been added include postmenopausal premenstrual, premenstrual crowded menopause, crowded menopause premenstrual, crowded menopause atrophic menopause, atrophic menopause crowded menopause, atrophic menopause, basophilic and atrophic menopause acidophilic. The vaginal smears were classified most frequently in subtypes acidophilic atrophic menopausal and regressive. Smears suspicious of malignancy were found most frequently in the regressive type and trichomonas vaginalis was most commonly associated with this type. The atrophic menopausal acidophilic group was least commonly associated with malignancy. Three of the malignancies were overlooked by cervical and vaginal smear; an error of 4.2 per cent. Nine, or 12.9 per cent, of the malignancies were diagnosed only by cervical smear. Trichomonas vaginalis occurred in 18.5 per cent of postmenopausal patients with malignancy. Seventy-seven per cent of all the malignancies were squamous cell carcinoma of the cervix.

VAGINAL CYTOLOGY OF POST-MENOPAUSAL WOMEN

STUDY II. ACIDOPHILIC ATROPHIC VAGINAL EPITHELIUM

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South. M. J., 41: 869-872, October, 1948

In this study the authors describe and discuss an additional vaginal smear subtype for postmenopausal patients. The vaginal and cervical smears of 68

women were found to belong to this group. The basal vaginal epithelium was characteristically acidophilic in reaction and illustrated various degrees of necrocytosis. The epithelial changes in the type of smear described are quite similar to those associated with necrobiosis and also to those resulting from action of podophyllin and colchicine on the skin. This type of smear was shown not to have a close correlation with malignancy. The accentuated degeneration illustrated in these smears may be secondary either to an endogenous hormonal imbalance or to an exogenous irritant such as infection. The latter is considered by the authors to be the less likely. 2 figures.

VULVO-PERINEAL EPITHELIOMA AND LYMPHOGRANULOMATOSIS

ALBERTO H. ROCHA

An. Bras. de Gin. 26: 167, 1948

A 56-year-old female sought medical treatment for an old, tender ulcerative lesion in the vulva, exhibiting rapid growth recently. Normal menopause had occurred 10 years previously. Pain was complained of on defecation, with elimination of blood and pus. Pelvic examination disclosed an ulcer localized in the vulvo-perineal region, measuring 5 cm. in diameter. Large hypertrophic tags were present around the anus and perineum. Rectal examination revealed an infiltrated mucosa and rectal stenosis. Frei test was positive. Biopsy revealed an epidermoid (spinal cell type) carcinoma and chronic hypertrophic proctitis. Patient was given radium treatment, followed by almost complete healing of the lesions within a month. She was discharged in good condition, but could not be traced for the past year.

The author believes, as this case tends to demonstrate, that lesions of lymphogranulomatosis predispose to the development of cancer. Several authors have already referred to this possibility, and numerous cases have been reported of cancer of the cervix coexisting with lymphogranulomatosis.

(Whether or not lymphogranulomatosis predisposes to the development of cancer, and it is quite possible that it may, there is no doubt that in a number of cases such an association or sequence has been noted. In a very recent case of lymphopathia venereum observed in the colored wards of the Johns Hopkins Hospital, the microscopic study of the ulcerated area showed definite cancer. A later radical operation with gland excision showed cancer metastases to the glands.—Ed.)

THE RATIONAL MANAGEMENT OF LEUKORRHEA

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M. Clin. North America 32: 1601-1610, November, 1948

Leukorrhea, an abnormal vaginal discharge, is probably the most common complaint of gynecological origin. This presentation discusses that type of discharge which is primarily annoying to the individual and has no serious organic basis. The two most common types of such leukorrhea are simple hypersecretion with normal vaginal flora and hypersecretion with abnormal flora and biology.

The normal vaginal secretion is just enough to moisten the external genitals and may be excessive at ovulation or before menstruation. The secretion is flaky, crumbly or granular and is greyish white or pearly in color. The composition of normal material is desquamated epithelium, glycogen, and aciduric bacilli.

A careful history and thorough examination must be a part of any approach to the management of leukorrhea. In simple hypersecretion there is found about the external cervical os heteroplasic cervical tissue in the form of areas of eversion, usually congenital in origin. This endocervical tissue is exposed to the acid vaginal secretion and produces an abnormal amount of mucus. If this is untreated, a cervicitis may develop. Treatment is based on the destruction of the heteroplasic endocervical tissue. Occasionally, leukorrhea occurring after pregnancy is caused by cervical tears which were induced by the trauma of labor and delivery, but the author feels that normal delivery does not produce eversions and that most such conditions are congenital.

If properly treated, eversions do not reoccur after delivery. The coagulating electrode of a diathermy machine is used for treatment. The glands are destroyed without injury to the underlying tissues of the cervix, and a mild antiseptic douche of a 1:4000 zephiran solution is used during the healing process.

When leukorrhea is caused by vaginal flora and biology, the secretion varies from normal to a dark brown or yellow in color. It is thin in consistency, containing pus cells and the *Trichomonas vaginalis*. Most often it will be alkaline, the glycogen content less and the vaginal membrane inflamed. Focal areas of infection in the lower genital tract or some endocrine imbalance may be suspected. Areas of infection can be recognized by examining the secretion from the tubules about the urethra and the ducts of Bartholin's gland for pus cells or by careful inspection of the cervix. The author feels that destruction or drainage is the preferred treatment for such conditions. A tissue coagulating machine with electrodes which will fit into the tubules can be used successfully.

The so-called trophic or senile vaginitis is characterized by a thin vaginal membrane with large areas of epithelial desquamation. An attempt should be made to change the chemical reaction of the vagina by the use of an acid douche.

Thyroid, estrogen or hormonal deficiency may account for a few cases of

leukorrhea. Yeast fungus infestation as a cause for leukorrhea in pregnancy is common. The author does not believe that *Trichomonas vaginalis* is necessarily responsible for vaginitis when other less easily recognized organisms could be responsible. The organism is commonly found in the vagina when the chemical reaction of the secretion is changed toward the alkaline. The best management seems to be the development of an acid vaginal secretion.

(Normally the cervical secretion is increased in quantity and decreased in viscosity at the ovulation phase, and one can note this even clinically in some women, especially in women free of any cervical infection which would vitiate such observations. In my experience the exudate is usually of thin mucoid character in contrast to the whitish, curdy character of the vaginal exudate seen in inflammatory conditions which increase the vaginal desquamation of epithelium. I have also noted that in a good many cases of functional bleeding of young patients, in which a persistency of the follicular estrogenic activity in the absence of progesterone is the immediate causative factor, complaint is made of a persistent thin mucoid discharge between the bleeding phases. This is obviously due to hyperactivity of the cervical glands. I doubt whether such simple non-infectious hyperactivity produces "areas of eversion," as the author states, and I believe that these small circular reddish granular areas around the external os are simply coincidental erosions of the so-called congenital or Fischel type. They rarely, if ever, call for any treatment. The term eversion or ectropion, as commonly used, refers to a mechanical rolling out of the endocervical tissue, usually the result of inflammatory swelling. The condition may be likened to the rolling out of the lining of a sleeve when it is too long for the cloth. I do not agree with the author that such eversions may not occur or reoccur after delivery. As a matter of fact, such ectropion is especially apt to be facilitated by the presence of the cervical lacerations so often noted after delivery.—Ed.)

VAGINAL CARCINOMA IN A GIRL 14 YEARS OF AGE TREATED BY RADIATION

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Am. J. Obst. & Gynec., 57: 396-397, February, 1949

This case is of interest not only because of its rarity, but also because it offers some additional data regarding the therapy for primary carcinoma of the vaginal wall.

The patient, a 14 year old girl, had begun what was thought to be menstrual bleeding 18 months before she was seen. The bleeding had become continuous though not profuse. An irregular, soft mass was palpated in the upper vagina. Microscopic sections showed advanced, medullary, squamous cell carcinoma.

The elevated portion of the growth was curetted away and 100 mgs. of radium was packed against the lesion. The radium was used in suitable containers, screened by 1 mm. brass and 1 mm. hard rubber. The first dose amounted to 3,600 mg. hrs. and was followed by supervoltage roentgen therapy.

The second series consisted only of supervoltage roentgen therapy. In the third series intravaginal radium was applied again. When the patient was last seen after 5 years, there was no evidence of recurrence.

(Many freakish cases of carcinoma of almost any organ at unusually early ages have been reported. I have not seen a vaginal carcinoma in a patient as young as 14, but recently I encountered an advanced carcinoma of the vulva in a girl of 20. The medullary nature of Siddall's case probably made it more radiosensitive than some of the more highly differentiated vaginal cancers. The radiotherapeutic problem in cancers of the vagina is often a rather delicate one, because of the risk of producing radium injuries of the bladder or rectum, especially the latter in view of the more frequent location of such growths on the posterior than on the anterior vaginal wall.—Ed.)

ENDOMETRIOSIS OF THE VAGINA FOLLOWING VAGINAL HYSTERECTOMY

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Am. J. Obst. & Gynec., 56: 1192-1194, December, 1948

Endometriosis is apparently relatively rare following vaginal hysterectomy, and in a brief review of the literature only one other case could be found. The case reported in this paper is that of a 39-year-old colored female, admitted to the hospital for excessive vaginal bleeding of one week's duration, with a past history of some menorrhagia for about 3 months. Pelvic examination revealed a small, nodular uterus; the remainder of the physical examination was negative. A vaginal hysterectomy without morcellation and a posterior colporrhaphy were performed and the patient made an uneventful recovery.

About 3 months after operation the patient noted the return of cyclic vaginal bleeding which was small in amount and which she interpreted as menses. Pelvic examination 2 years later showed a small, flat bluish area, about 4 by 6 mm., on the left posterior vaginal wall, immediately below the hysterectomy scar. A biopsy revealed endometriosis of the vaginal vault. It was felt that it was quite probable that the endometrium was implanted during surgery. 2 figures.

(This is, as the authors state, an almost unique observation, but it would seem hazardous to attribute the small area of vaginal endometriosis to operative implantation, as the authors at least tentatively suggest. The uterus had been removed intact and without invasion of its cavity at the operation more than 2½ years ago. Moreover, vaginal endometriosis can occur even in the absence of ovarian endometriosis, while the latter can apparently not be excluded in this case, even in the absence of palpatory findings. The photomicrograph accompanying the paper leaves no doubt of the genuinely endometrial nature of the vaginal lesion.—Ed.)

TECHNIQUE FOR ISOLATION, MAINTENANCE AND MASS CULTURE
OF DÖDERLEIN'S BACILLUS

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Am. J. Obst. & Gynec., 56: 1104-1110, December, 1948

The presence of the Döderlein's bacillus in the female vagina is considered normal and in fact this organism probably plays a role in the maintenance of the normal vaginal pH. The purpose of this study was to find an improved medium which would successfully maintain these vaginal bacilli in prolonged culture and provide a possible harvest of mass cultures so that continued investigation could be carried out. The medium which was found to be most satisfactory was composed of phytone, 2 gm.; dextrose, 1 gm.; distilled water, 90 cc.; and human serum, 10 cc. The addition of 1.5 gm. of agar provided a solid medium. Phytone is an enzymatic digest of soybeans, cottonseeds and peanut meal. Other organisms were usually inhibited by the acidity of the broth and the Döderlein's bacillus could be isolated by streaking on the agar preparation and then picking out single colonies.

The growth of this organism was compared with *Lactobacillus acidophilus* on the phytone medium and in litmus milk and carbohydrate fermentation tubes. It could not be differentiated from *L. acidophilus* in these media. Biochemical and serological differentiations could not be made with this medium. The thermal death point for Döderlein's bacillus was 72 degrees C. for 20 minutes in the absence of blood serum. 11 figures.

THE UTERUS

THE HISTOLOGY OF THE ENDOMETRIUM IN "FUNCTIONAL UTERINE HAEMORRHAGE": ANALYSIS OF 1000 CASES AND REVIEW OF THE LITERATURE

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Glasgow M. J., 30: 1-28, January, 1949

The writer has analyzed the histological findings in 1000 cases of abnormal uterine bleeding in the absence of gross pelvic pathology. All patients with bleeding after the menopause were excluded. Various minor gynecological lesions were present in many of these patients; however, none of these minor lesions was capable of producing uterine bleeding. In 139 instances, lesions were found on routine endometrial curettage. Prior to the curettage, none of these cases was suspected to have organic disease, a fact which demonstrates the necessity of diagnostic curettage in all cases of presumed functional bleeding, irrespective of age. The organic lesions found were as follows: chronic endometritis occurred in 110 cases, uterine polypi in 11 cases, tuberculosis in 10 cases and malignant disease in 8 cases.

In the remaining 861 cases no organic pathological conditions of the endometrium were found. Endometrial hyperplasia occurred 265 times, endometrial atrophy 10 times, irregular shedding of the endometrium 13 times and irregular ripening of the endometrium 26 times. In the remaining 547 specimens the endometrium appeared normal. The incidence of these various alterations is for the most part in agreement with the reports of other large series, with the exceptions that atrophic endometrium and irregular ripening and shedding are thought to be somewhat more common than this report would indicate. In those cases in this study in which the endometrium appeared normal, 284 showed endometrium in the proliferative stage and 263 instances in the secretory phase.

In 48 patients additional specimens were studied and it was found that a portion of the patients showed a different type of endometrium on subsequent examinations. Of those who on the first examination showed normal endometrium, 6 on subsequent curettage showed hyperplasia, one showed chronic endometritis and one showed carcinoma. Five patients who on the first examination showed hyperplasia later had normal endometrium. One patient revealed a change from atrophic endometrium to hyperplasia on a second examination.

Attempts to correlate the histological appearance with the type of bleeding and with the findings on pelvic examination failed to demonstrate any relationship in either instance. It was finally apparent that almost any type of abnormal uterine bleeding can occur from any type of endometrium, and that any attempt at diagnosis of functional bleeding without histological examination of the endometrium is quite unjustifiable.

(This interesting statistical study of endometrial findings in association with bleeding yields incidences of various endometrial pictures which I should offhand say are approximately what most of us would expect. Especially interesting are the findings in the 861 cases of functional bleeding. In 547 specimens the endometrium was described as normal, but most of the 284 which showed proliferative pictures can probably be added to the 265 with genuine hyperplasia to represent a group of 549 in which the bleeding was probably of the anovulatory type, corresponding to the older designation of "metropathia hemorrhagica," as applied in the original study of the subject by Schröder in 1915. This assumption may not be accepted by the author, as its accuracy would depend upon the stage of the cycle in which the endometrium was obtained. Even with this maximum estimate, however, it is surprising that as many as 263 cases showed a secretory picture, a proportion which I suspect is higher than most of us have encountered. In any event, the old dictum that functional bleeding can occur from any histological type of endometrium is borne out by Sutherland's studies.—Ed.)

OBSERVATIONS ON THE CRYSTALLIZATION OF THE CERVICAL MUCUS

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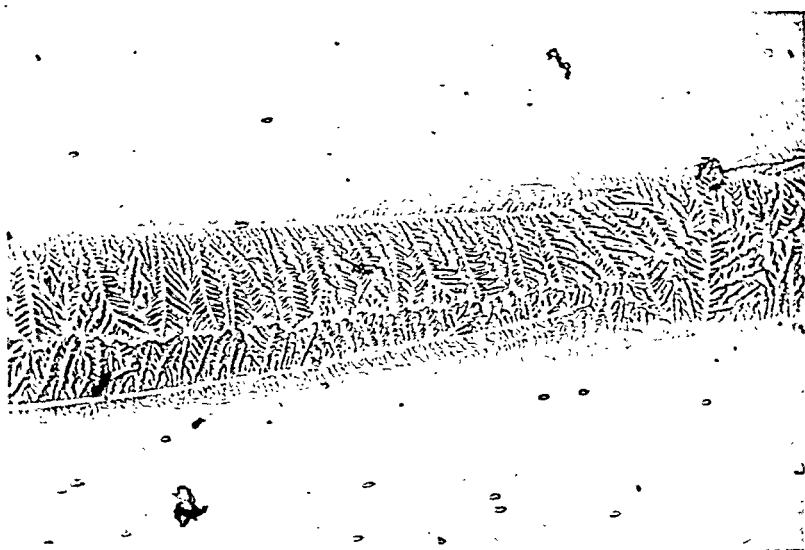
Acta obst. et gynec. Scand., 28: 172-187, 1948

If a drop of cervical secretion is dried and then examined under a microscope, varying amounts of crystal formation may be observed. The extent of crystallization is greatest when the mucus is limpid, glass-like and stringy, at which time massive, lattice-like formations occur. At other times of the cycle the formation is thinner, smaller and less regular and, as a rule, the smallest amount of crystals is seen in the days immediately before menstruation. The appearance of these crystals is reproduced in microphotographs accompanying this paper.

It has been found that the crystals consist of sodium chloride and that the characteristic forms which they assume depend upon the presence of mucin substances. Quantitative determinations of the amount of NaCl in 2 samples of cervical secretion of the glass-like, thinly liquid type showed that the amount corresponds to that present in a so-called physiological salt solution. Crystal structures strikingly like those in cervical mucus were produced by letting a solution of ordinary egg albumin, to which 0.9 per cent of NaCl had been added, dry on a slide. When about the same volume of 0.9 per cent NaCl was added to saliva, one observed rather massive formations of precisely the same appearance as those found in cervical mucus. The constant type of crystal formation and of the physical properties of the cervical mucus in the days close to ovulation favor the idea that this amount of salt is rather constant at the time of ovulation, and it seems natural to assume that it is of importance to the physico-chemical properties of the mucus and hence to its physiological function.

Whether the actual secretion of the cervical glands is qualitatively different in the various phases of the cycle is still open to question. One may imagine that

the difference in the amount of visible crystals in the dried preparation simply depends on the fact that the cervix content in the premenstrual phase consists



to a large extent of detritus, cellular elements and liquid components having another origin than the cervical glands themselves.

The author shows why the "argyrophil secretion" mentioned by Papanicolaou

finds its explanation in these salt crystals. The argyrophil secretion was described as one which stains brown or yellow with silver nitrate, producing "anastomosing branches with heavily indented leafy projections." It is plain that these structures with the characteristic arborization originate from the salt crystals formed at the drying of the sample; there has occurred a precipitation of silver chloride which more or less exactly reproduces the original form of the crystals, and in the subsequent exposure to light metallic silver has by reduction been formed on the precipitate. 9 figures.

(The author of this paper is the Director of the University Clinic of Obstetrics and Gynecology at Copenhagen, and, through a recent visit to some of our clinics, is known to many American gynecologists. He has long been identified with problems of reproductive physiology, and has made many contributions in the field of treatment of various functional disorders. The paper abstracted above presents a new approach to the study of variations in the composition of the cervical mucus, and the graphic nature of the sodium chloride crystal findings is well illustrated in the accompanying figures. The author himself is very conservative in his interpretation of the significance of these findings, and very properly cautions that the varied crystalline pictures may not be an index of qualitative differences in the actual cervical secretion, especially as such adventitious elements as cellular debris and exudates not actually of secretory origin must be considered. However, his results may lead others to more intensive investigations by this technique.—Ed.)

ENDOMETRIOSIS AS A CAUSE OF ILEAL OBSTRUCTION

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Am. J. Obst. & Gynec., 56: 1059-1068, December, 1948

An analytic study of the clinical data in 16 cases of ileal obstruction caused by endometriosis is presented. Three of these cases were from the files of the Mayo Clinic and 13 were from the medical literature. The signs and symptoms of this condition are a combination of those of either of the diseases seen separately. Sterility of more than 10 years' duration, increasing acquired dysmenorrhea and menstrual periodicity in the symptoms of endometriosis and progressive ileal obstruction were frequently encountered. The more direct symptoms of obstruction included abdominal pain, abdominal distention, vomiting, obstipation and the palpation of a mass. The discovery of tender nodules in the cul-de-sac of Douglas or along the uterosacral ligaments and the presence of uterine fibroids or ovarian cysts may be helpful in arriving at a diagnosis. Obstruction of the distal part of the ileum by endometriosis often has been thought clinically to be appendicitis accompanied by ileus. The symptoms of endometriosis generally can be elicited, however, if a thorough history is taken. The clinical picture of ileal obstruction caused by endometriosis is much less characteristic than that of sigmoidal obstruction.

The treatment of choice in ileal obstruction is ileal resection, with or without preliminary ileocolostomy or enterostomy, and with or without bilateral oophorectomy and/or hysterectomy. Each case must be individualized, depending on the amount of pelvic disease which is associated with the obstruction.

The mechanism of ileal obstruction was found to be due, usually, to kinking caused by adhesions of endometriosis and, to a lesser degree, to the impingement of the endometrioma into the intestinal lumen. Endometriomas of the ileum were more superficial in location than those of the pelvic part of the colon.

Microscopically, reactive fibrosis around the endometrial glands and stroma was characteristic. Endometrial glands and stroma were found in all layers of the intestinal wall except the mucosa. They were more prominent, however, in the muscularis propria and the serosa. Histopathologic examination of frozen sections of tissue and pathologic confirmation of endometriosis as the cause of ileal obstruction are imperative in every case, because a malignant process can be excluded only by this method.

(Ileal obstruction by endometriosis is seen usually in association with pelvic endometriosis, which may be either moderate or extensive in degree. On the other hand, in the exceptional case, it may occur in the entire absence of demonstrable endometriosis of the ovaries or other pelvic organs. Such cases pose a difficult problem at the operating table, because the surgeon is far less likely to think of endometriosis than of the more common carcinoma. I have seen one such case, in which the intestinal lesion was noted in the course of a hysterectomy for uterine myoma, and with no sign of endometriosis in the pelvis. The picture was that of a typical annular carcinoma, and resection was performed. The microscopic examination showed typical endometriosis but no carcinoma. As soon as the intestinal segment is removed in such cases, naked-eye examination of its interior wall excludes cancer, since the mucosa is smooth and normal in appearance. As the authors state, the endometrium commonly involves the muscular and serous layers of the bowel.)

In the more common variety of intestinal involvement by endometriosis, the presence of very obvious pelvic endometriosis would be more likely to lead to the suspicion of the same lesion in the bowel, but even here resection is the treatment to be performed, certainly in those women during reproductive life in whom the treatment of the pelvic disease is to be along conservative lines, with retention of ovarian tissue. Even if a radical pelvic operation is done, resection, sometimes preceded by ileostomy, must of course be done in the presence of an existing acute obstruction. Moreover, when obstruction has not yet developed, one can not be sure that this will not occur before the comparatively slow regression of the endometrial tissue after ovarian ablation, or that the regressed fibrotic endometrium may not still be a menace to the patient.

Far more common than ileal involvement is infiltration of the rectum and sigmoid, often producing a pseudo-neoplastic appearance and sometimes even a complete obstruction which will necessitate colostomy. However, rarely is there any justification for the formidable resections which were at one time recommended and practiced for these cases. Complete ablation of ovarian tissue is indicated, and when this is technically impossible post-operative radiation will always bring about regression of the intestinal endometrium. There is reason to believe that recognition of this fact is not yet universal among the general surgeons who often see these patients. Only a few weeks ago I saw in consultation a patient in whom a recent operation by a well-qualified gynecologist had shown extensive endometrial involvement of the rectum, but in which the operator felt sure that all ovarian tissue had not been removed because of the technical difficulties encountered. A general surgeon who saw the patient after operation had strongly urged resection, which would, I believe, have been a difficult, hazardous and unnecessary procedure.—Ed.)

A FURTHER CASE OF STROMAL ENDOMETRIOSIS

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AND

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J. Obst. & Gynaec. Brit. Emp., 55: 423-427, August, 1948

There have been 35 reported cases of a diffuse type of new growth of the uterus in which the abnormally situated tissue bears a morphological semblance to endometrial stroma. To this growing list of case reports, the authors have added another example.

The patient, a 39-year-old married female, was admitted to the hospital complaining of a dull-aching pain in the right side, of one year's duration. On two occasions the pain had become severe but it was never associated with any gastrointestinal symptoms. In the year prior to hospitalization there had been some excessive menstrual loss. She had had 2 normal pregnancies.

On examination there was a large firm symmetrical swelling in the midline extending from the pubis to just below the umbilicus. The mass was freely movable from side to side. On vaginal examination the uterus was enlarged to the size of a 4 months' pregnancy and was of a firm consistency. There was some thickening and tenderness in the right fornix. A laparotomy was performed, and the uterus was found to be symmetrically enlarged. The right ovary showed several small follicular cysts. In the right broad ligament there were 2 tortuous fingerlike projections extending from the lateral margin of the uterus outwardly. A supravaginal hysterectomy and a right salpingo-oophorectomy were performed, and the upper of the 2 projections was removed. The lower one could not be entirely dissected. Postoperatively, the patient did well and was discharged from the hospital. Two months later she was given a course of deep x-ray therapy and one year later she was still in good health.

On cut section the myometrium was studied with a mass of small dome-shaped protuberances 2 to 5 mm. in diameter and consisted of smooth, firm white tissue. There was an irregular fibrous trabeculum. In the posterior wall of the uterus there was one cystic cavity the size of a walnut which was occupied largely by a pedunculated mass of firm white tissue. The uterine cavity was narrowed and one small polyp was present. The mass in the broad ligament was composed of thick cords of infiltrating tissue.

On microscopic section, the endometrium appeared normal and the ovary showed several simple follicular cysts. The abnormal tissue of the uterus was made up of indistinct, faintly eosinophilic cells. The nuclei were round and clearly seen and mitoses were scant and of normal type. There was absence of any polymorphism. The growth appeared to be of completely undifferentiated stroma-cell type. The tissue was only moderately vascular. In some areas there was an

arborescent pattern of abnormal cells which bore a resemblance morphologically to the primitive sex cords.

The authors feel that definite proof that the tumor was derived directly from the endometrium is still lacking, though morphological evidence seems to favor this possibility. It is also possible that the tumor tissue and endometrium have a common ancestor and that the process is a neoplasm proper, having its origin in partly differentiated tissue of embryonic bipotency lying indiscriminately throughout the uterus. 10 figures.

(An increasing number of these interesting cases of stromal endometriosis or stromal adenomyosis, or stromatosis, as they are variously called, is being reported, though the lesion must still be considered a rare one. A remarkable feature of some of these cases is the tendency to endolymphatic and endovascular penetration, and the local invasiveness of the stromal tissue is often shown grossly by the presence of such finger-like projections into the broad ligament as the authors describe in their case. An even more marked invasion of the broad ligament was seen in a case recently studied in our laboratory, and this had made the operation one of great technical difficulty. While such stromatosis, like adenomyosis, may be seen in association with myomas, the latter are perhaps more often absent, and the gross appearance of the enormously and diffusely thickened, trabeculated uterine wall is somewhat like that seen with adenomyosis. A malignant form of the same lesion has been described, but it seems to me that no line can be drawn between this and endometrial sarcoma. As for the origin of the stromal tissue of the lesion, there would seem little doubt that this is from the endometrial stroma, and that there is no need to invoke the embryologic hypothesis suggested by the author.—Ed.)

ENDOMETRIOSIS

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Perth, Australia

M. J. Australia, 2: 412-414, October, 1948

This writer describes the condition of endometriosis, the symptomatology, diagnostic features and treatment. The chief symptoms are dysmenorrhea, sterility, rectal pain and pain on defecation, irregular uterine hemorrhage (which might not be present) and lower abdominal pain. In diagnosis, it is important to use a vaginal speculum, to discover the presence of hypertrophy of the cervix and of blue-domed cysts, particularly in the posterior fornix. On bimanual examination, movement of the cervix away from the site of the lesion will generally elicit pain. The palpation of small, hard, tender nodules in the posterior fornix is significant. Attempts to replace the retroverted uterus will cause acute pain if the utero-sacral ligaments and posterior vaginal fornix are involved. Referred pain will be felt in the rectum if the rectal wall is involved. A barium enema will aid in differentiating rectal involvement from carcinoma of the rectum. Treatment will depend on the extent of pelvic involvement, age of the patient, and any associated sterility. Young women may be treated by injections of testos-

terone propionate for temporary relief, but this may tend to produce masculinization. Surgical treatment must be resorted to in the majority of cases, and conservation should be observed as far as possible. Deep x-ray therapy to inactivate the ovaries should never be used except when the condition is inoperable.

(This paper contains nothing new, but presents a short résumé which should be of service to the general practitioners who make up the bulk of the readers of the journal in which it is published.—Ed.)

POSTMENOPAUSAL CYSTIC GLANDULAR HYPERPLASIA OF THE ENDOMETRIUM

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An. Bras. de Gin. 26: 189, 1948

Cystic glandular hyperplasia of the endometrium was until recent years considered exclusively a lesion of reproductive life. It is now well known, however, especially in view of the recent contributions of American investigators (Novak, Richardson and others), that endometrial hyperplasia may develop many years after the menopause. This finding, of course, modified the former traditional concept that postmenopausal bleeding justified the assumption that cancer should be present somewhere in the female genital organs. As to the source of the estrogenic hormone responsible for the growth of the postmenopausal endometrium, Novak points to the adrenal cortex and pituitary as probable sources of the hormone, although the ovary itself may continue to produce estrogen after the menopause. Wallart, studying 60 cases of endometrial hyperplasia, encountered 19 in women beyond the menopause, the ovaries of which showed a well preserved cortex and conspicuous corpus fibrosum and rete elements. He considers the interstitial gland of the ovary, the rete, para-ganglionic tissue and corpus fibrosum of the ovary as the possible main sources of estrogen after the menopause. Contrary to the viewpoint held by histologists, the corpus fibrosum should not be considered as simple scarlike structure. Unlike ordinary scar tissue which tends to disappear sooner or later, the structure of corpus fibrosum maintains its earlier characteristics throughout years until late age. Moulounguet and Doleris believe that postmenopausal hyperplasia is due to reactivation of a senile uterus from an ovarian source. Even beyond the menopause it is possible for small follicles to undergo maturation, even though the latter may only be partial.

Case report: a 60-year-old female sought medical treatment for vaginal bleeding lasting for 6 months. Normal menopause had occurred 15 years previously. Pelvic examination disclosed an extremely atrophic vagina and an abdominal cocoa-nut-sized mass, irregularly outlined, hard, slightly movable and filling the pelvic cavity. The adnexa could not be outlined. Cervical examination and

curettage could not be done due to the existence of a sharp, irremovable, ring-shaped stenosis of the vagina. Laparotomy revealed a soft, enlarged uterus (two-month pregnancy size) and both ovaries enlarged. One ovary was the size of an orange, and the other double this size. Both were cystic. Tubes were normal and free. Panhysterectomy with bilateral salpingo-oophorectomy was performed, and the pathological report disclosed cystic glandular hyperplasia of the endometrium, adenomyosis, several follicle cysts with intact granulosa cells and numerous corpora albicantia. In this case, therefore, the ovaries were of the functioning type.

Every case of postmenopausal bleeding unaccompanied by cervical, uterine and adnexal lesions, is very suspicious of endometrial hyperplasia. Endometrial biopsy will furnish the correct diagnosis and guide the specialist in the treatment accordingly. Granulosa cell tumors, thecoma and luteomas ought to be ruled out very carefully, and this quite often constitutes a difficult histologic problem.

(There is good evidence that the adrenals, in addition to various other hormones, produce an estrogenic endocrine factor. Aside from this, the fact that estrogen has often been found in the urine many years after total ablation of ovarian tissue would seem to be pretty good evidence that the source of postmenopausal estrogen is not in the ovaries but in some other endocrine gland, probably the adrenal cortex. It is probably quite true that the cessation of menstruation does not mean an abrupt cessation of ovarian function, and that follicles may continue to develop to various stages for a time, probably a comparatively short time, after actual termination of menstrual life. On the other hand, the histologic structure of ovaries many years after the menopause does not suggest the probability of a persisting function, nor do I know of any evidence to support the hypothesis that very old corpora fibrosa or albicantia possess any secretory function. While these structures are histologically demonstrable for many months, they tend to be gradually blotted out, and I can not believe that a corpus albicans, for example, would persist in histologically demonstrable form, much less as a functioning structure, for anything like 15 years after rupture of the follicle, of which it is a residue.

If the author is correct in his description of follicle cysts with intact granulosa in association with the endometrial hyperplasia, after 15 years of amenorrhea, one would be inclined to assume that the case might be one of delayed menopause, with an abnormally long amenorrheal interlude. Moderate degrees of such a disorder are fairly common, and hyperplasia of the endometrium is a not uncommon finding in postmenopausal bleeding occurring perhaps a year or even longer after the menstrual function was thought to have ceased. In this sense it would certainly be true that some cases of postmenopausal hyperplasia are actually due to abnormal persistence of ovarian estrogen function. No one can be arbitrary in this point, and it seems that, for reasons above mentioned, the factor of extraovarian estrogen production is probably the important one in many cases.—Ed.)

ACUTE DECIDUAL ENDOMETRITIS AND METRITIS

M. M. ALTER

Bull. Margaret Hague Maternity Hosp., 1: 107-109, December, 1948

Acute decidual endometritis and metritis is a post-abortion or post-puerperal condition due to infection of abnormally developed decidua. A case is presented

in which a 19-year-old primipara began to have morbidity and bleeding 8 days after delivery. The uterus was the size of 8 to 10 weeks normal gestation. Pathological findings of curettage showed no evidence of chorionic villi, but infected decidual masses with inflammatory reaction involving the subendometrial uterine wall.

It is estimated that the average incidence of this condition is about one per cent. The patient may be more or less symptomless during the early puerperium, later to have abnormal lochia and bleeding. If the lesion is confined to the abnormally developed uterine lining and affects only the superficial layers of the subendometrial fibromuscular wall, curettage will effect a cessation of the process. However, if there are further pathological changes in the deeper tissues of the uterine wall, the process may progress to more severe degrees, depending on the degree of infection and the degree of degenerative changes in the fibromuscular wall. 1 figure.

(The lesion described by the author is found much more frequently after abortion or miscarriage than after full term delivery, just as clinically curettage is far more frequently done after the former than after the latter. The histological picture of the lesion found after miscarriage is dependent upon the amount of retention of gestational tissue and the time which has elapsed since the miscarriage. In some cases one finds considerable numbers of actual placental villi, but in the later stages perhaps only an occasional old fibrotic or hyalinized ghost villus. Again, there may be considerable areas of infected decidua, or there may be little or no trace of the original decidual reaction, but instead varying degrees of chronic endometritis. Other features, such as traces of the Nitabuch layer of canalized fibrin, hyalinization around the blood vessels, or scattered trophoblastic cells, may or may not be present.

After full term delivery, retained placental tissue is less common, though trophoblastic invasion of the decidua may persist in the form of a syncytial endometritis or deciduitis. The decidual reaction of the stromal cells may persist for a considerable time, with practically always evidence of infection and chronic inflammation, this apparently being the lesion which Alter has in mind. As he says, persistence of the condition may be followed by extension of the chronic inflammatory condition to the muscular layer in the form of a chronic myometritis.—Ed.)

VAGINAL CERVICAL SMEAR IN THE DIAGNOSIS OF UTERINE CANCER

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Richmond, Virginia

Virginia M. Monthly, 75: 468-474, November, 1948

In the authors' experience, the Papanicolaou stain and cytological study of the vaginal and cervical smear has provided a satisfactory means for screening large numbers of patients in an effort to make the diagnosis of uterine cancer before

clinical symptoms or signs lead one to be suspicious. In the present series, a total of 1320 patients were screened and 28 cases of proved carcinoma were found. There were 24 cases with carcinoma of the cervix or fundus in whom the clinical history or pelvic examination made the diagnosis apparent or aroused suspicion to the point where biopsy and curettage were done. In all of these cases the vaginal smear was positive for cancer cells, but these cases would have been diagnosed without the vaginal spread. Four cases of unsuspected, asymptomatic cancer of the cervix are reported in some detail, and in these cases routine vaginal, abdominal and speculum examination had failed to arouse suspicion of the lesion. The diagnosis was made on the basis of the vaginal smear and confirmed by biopsy or by pathological study of the removed tissue. In one case in which the smear was suspicious, multiple sectioning of the uterus after panhysterectomy failed to reveal any malignancy.

(There is apparently no end to the spate of papers dealing with the vaginal smear method in the diagnosis of uterine cancer, and it is difficult to avoid repetitiousness in commenting upon them, since the subject has been discussed so many times in these pages. Everyone is agreed that cancer is an exfoliative lesion, and that the vaginal smear is of great value as a screening method, but not one of sufficient diagnostic decisiveness to be used as the basis of treatment. Nor can it distinguish between the clinically benign intraepithelial lesion and the genuinely invasive cancer which is of course always clinically malignant. The precursory and very early subclinical invasive lesions are relatively rare, making up only a tiny fraction of all cases of cancer. Some of us feel that vaginal cytology has been unduly and disproportionately accented and publicized, even in the popular press, tending to incite a demand for vaginal smears which simply can not be fulfilled in view of the extreme paucity of real experts in cytology, and the enormous amount of time and money involved. There is still much haziness of viewpoint as to the sequential and chronological relations of pre-invasive lesions and real invasive cancer, and many feel that more lives can be saved by increasing the proportion of the therapeutically favorable Stage 1 cases than can be saved by the recognition of precursory lesions, in the treatment of which many therapeutic sins have already been committed. Moreover, vaginal smears are not necessary in the diagnosis of Stage 1 cases, in which direct biopsy gives an accuracy of more than 99 per cent, although there can be no criticism of the supplementary employment of vaginal cytology. No one can at this stage be sure the future niche to be filled by the vaginal smear technique. It may very gradually be superseded or curtailed by some much simpler screening test, such as the blood test devised by Huggins, which of course still awaits confirmation. There are still wide differences of opinion among gynecologists as to the ultimate value and applicability of vaginal cytologic diagnosis. As against the enthusiasm of the proponents, such a good pathologist and experienced clinician as Robert T. Frank has in a recent paper (*Am. J. Obst. & Gyn.* 57: 341, 1949) spoken of the "somewhat hysterical overanxiety to ferret out cervical cancer in situ or often only in prospect," and has deplored the picture of "women racked by unjustified fears, anxieties, and premonitions of disaster caused by the witch-hunter attitude of the professional cancer tracker." Such terms as "witch-hunter" and "professional cancer-tracker" seem pretty strong, and I do not think they would be endorsed by those of us who feel that the intensive study of very early cancer stages is always highly desirable. But there is a nugget of justification in Frank's sardonic criticism. In a still unpublished paper of my own, I have tried to evaluate this new field of diagnosis and cancer, but I have no hope that the ideas expressed, of which the above are samples, will pour oil on the troubled controversial waters in this field, and I shall probably be "smeared" as a reactionary by my good friends, the cytologists.—Ed.)

AN EVALUATION OF THE CYTOLOGY TEST FOR UTERINE CANCER

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M. Clin. North America, 32: 1563-1572, November, 1948

A summary is made of experience gained over a 5-year period during which more than 20,000 smears have been studied. Particular reference is made to the many factors in technic and interpretation which tend to influence its accuracy, diagnostic value and usefulness. Various possible points of error in the methods of collection, fixation and staining are discussed. There are no absolute criteria for making a positive diagnosis of malignancy. Instead, abnormalities of the nucleus, changes in the cytoplasm and associated findings must all be evaluated properly.

A résumé of reported statistics is given and mention is made of the wide variation in false positive and false negative percentages reported in different studies. The relative value of the smear in various types of pelvic malignancies and in carcinoma-in-situ is discussed. The relationship of the smear to the biopsy is a complementary one.

A TECHNIQUE TO AID IN THE DETECTION OF MALIGNANCY OF THE FEMALE GENITAL TRACT

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Am. J. Obst. & Gynec., 57: 274-281, February, 1949

A number of primary assumptions underlie the application of direct current measurement to a cancer problem. The first is that the living system possesses an electrodynamic field. The second, variations in biologic activity are correlated with electrical characteristics in the field. These variations can be measured by determination of standing potential differences. The authors describe a technique for the application of such a determination to the problem of cancer detection. They feel that cancer represents the breakdown of the forces of organization within the electrodynamic field.

A brief summary of 428 cases upon whom the technique was used is presented. In 75 patients with cancer of the genital tract, 74 showed the cervix to be electronegative. Of 353 nonmalignant patients, 81.9 per cent showed electropositive. From this nonmalignant group 18.1 per cent showed electronegativity similar to cancer. It is suggested that these patients should be carefully followed. 3 figures.

(Cancer detection and screening tests are popping up pretty frequently these days even more so than the cancer cures which in the past have appeared in the newspapers with such regularity. The simple electrical test suggested by the authors sounds almost too easy and too good to be true, and it will of course need a powerful lot of confirmation before it can be accepted. Many will recall the hope held out a few years ago for the detection of the time of ovulation by means of the electropotentiometer, as I believe the instrument was called, but the method just didn't pan out. A number of sound investigators have made conservative preliminary reports of simple chemical methods which they believe may prove to be valuable in determining the presence of cancer somewhere in the body. At this writing I have seen no publication in any scientific journal of Huggins' blood coagulation test, so widely publicized in the newspapers, which every medical man must nowadays read in order to keep abreast of his patient. However, the high scientific standing of the author of this test, and the fact that it apparently created much enthusiasm in the highbrow scientific organization before which it was presented, encourages one to hope that its accuracy will in due time be established. What a milestone in the cancer campaign this would be! Another test, based on a different concept, that of enzymes, is being studied in the clinic of Dieckmann, another scientist of demonstrated accomplishment. As a distinguished obstetrician, he can be sure that his obstetrical and gynecological colleagues will be rooting for him to deliver the goods.—Ed.)

OBSERVATIONS ON THE DELAY PERIOD IN THE DIAGNOSIS OF PELVIC CANCER

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M. Clin. North America 32: 1573-1581, November, 1948

The Committee for the Study of Pelvic Cancer is working in Philadelphia to determine the factors and responsibility in the delay period occurring in pelvic cancer cases. Material is obtained from living cases and the physicians consulted by these patients. The purpose here is to analyze the reasons for physician delay and to offer constructive suggestions whereby the delay may be avoided in the future.

In an analysis of 1000 cases taken from several Philadelphia hospitals, physician delay occurred in 276 instances. Curiously enough, cancer of the vulva, the most accessible lesion, experienced the longest delay.

Factors playing a part in physician delay are presented. Incorrect diagnosis is criticized only on the basis of failure to employ available diagnostic aids when indicated.

The greatest single factor for which the physician can be criticized is failure to do a pelvic examination in the presence of pelvic symptoms. This occurred in 142 cases of the 276 and cannot be passed off lightly. The presence of vaginal bleeding was given by many as a reason for deferring the pelvic examination. There is no reason for not examining a patient under these circumstances, and irrevocable time may be lost. Many cases indicated that pelvic symptoms were

treated without an attempt at diagnosis. Medication in any form for symptomatic relief is to be condemned until effort has been made to establish a diagnosis. Failure to examine the patient at the first office visit is a major cause of delay. Such casual treatment leads the patient to interpret the condition as a minor one and many times to disregard any further treatment. Medication should not be given to any patient who refuses an examination. The willingness to ascribe most any symptom in the 40-55 age group to the effect of the menopause is a common practice. A patient visited at home must and can be given a pelvic examination in the home.

A diagnostic delay in examined cases may result for several reasons. Failure to carry out routinely a complete pelvic examination results in delay. The wide and indiscriminate use of hormones contributes frequently to errors in diagnosis.

Failure to institute adequate therapy has contributed to results comparable to those from delayed diagnosis. *Inadequate therapy, either surgery or irradiation* in the presence of a known cancer, is inexcusable. When referring a cancer patient, the physician must take responsibility in seeing that prompt contact is established.

(Philadelphia was the pioneer city in the inauguration of the Maternal Death Conferences which have now been adopted in most of the larger cities of the country, with a definitely improving effect upon standards of obstetric practice. The same city now takes the lead in the investigation of the causes of delay in the diagnosis of pelvic cancer and thus puts up another target for other cities to shoot at, if I may assert my independence by ending a sentence with a preposition if it looks happiest and most comfortable in this position.)

It will probably not surprise gynecologists to read that in 142 of 276 cases no pelvic examination had been made by the attending physician. This in itself would not be a terrible omission, since many general practitioners feel rather incompetent in such examinations. But the unpardonable thing is that the physicians have not insisted that the patient have an examination by some one qualified to make it competently. Certainly every doctor must know that abnormal bleeding may mean cancer. It is not pure ignorance, but a peculiar apathy and a lack of conscientiousness which must explain why the doctor can be content until such a problem is fully investigated. We are doing a powerful lot of education of the public these days, but the skirts of our own profession are far from clean, and there is still much room for education and exhortation within our own ranks.

Another point which can be underscored is the hazard of endocrine therapy in abnormal bleeding before the nature and cause of the bleeding has been determined. Every gynecologist can think of cases where bleeding has been treated by hormones, often in the form of "shots," and in which a simple pelvic examination would have revealed a definite structural lesion, all too often malignant. I recall a young woman of 35 who had thus been given "shots" for nearly one year, when the mere vaginal insertion of the finger would have revealed the carcinoma of the vaginal wall from which she subsequently died. More power to our Philadelphia colleagues in this promising new undertaking!—Ed.)

RETREATMENT OF CARCINOMA OF THE CERVIX

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South. M. J., 41: 902-906, October, 1948

Medical opinion differs widely as to the need for, and advisability of, additional radiation treatment of carcinoma of the cervix, after the initial course of treatment has been completed. The author has analyzed 500 consecutively treated cases in order to evaluate supplemental radiation therapy. The average initial radium dosage was 4500 milligram hours and the x-ray dosage 2200 to 2300 r.

Of the 500 cases observed, 233 were felt to need therapy in addition to the initial radiation. In 50 patients the results of the initial treatment were unsatisfactory. Forty-seven of these patients had tumors which were graded as belonging to Group III and IV. In only one case in which secondary treatment was given were any beneficial results obtained.

In a second group of 110 cases the initial treatment brought about marked improvement; however, at check-up examinations there was evidence of persistent carcinoma. Ten of the cases in this group were made definitely worse by supplementary treatment. However, on the other hand, 27 of these 110 cases who had evidence of persistent cancer lived 5 years or more after subsequent radiation.

The third group of patients, 73 in number, were thought to have completely satisfactory eradication of the pelvic lesion, but at a later date showed a definite recurrence in the pelvis or in some other part of the body. Of these 73 patients with proved recurrences, 7 lived 5 years or longer after follow-up radiation.

A total then of 20 lives would seem to have been saved as a result of retreatment of these 233 cases. The author feels that whatever saving there actually was in the present group must be attributed to careful follow-up examinations at regular intervals. He feels that retreatment, whether supplemental or for frank recurrences, is eminently worthwhile.

(This is a valuable paper, calling attention to the fact that even when recurrence occurs after irradiation, there are still things to be done to prolong the patient's life very materially and that re-irradiation is often a valuable second line of defense against the disease. There are few experienced gynecologists who have not observed patients who have thus survived even for a good many years after secondary radiotherapy. A careful and conscientious follow-up is not to be looked upon as merely an essential in the evaluation of the results of the primary therapy, but as a continuing protection for the patient.—Ed.)

TREATMENT OF CERVICAL CANCER IN LOCAL
TUMOR CLINICS

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AND

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South. M. J., 41: 909-912, October, 1948

In two county medical society tumor clinics the incidence of cervical cancer has been found to rank high on the list of malignant disease. In these clinics the diagnosis of such tumors has been made by biopsy, though vaginal smear technique has been used for screening purposes. It is felt that the treatment of choice in small clinics such as these is irradiation in all cases except those in the pre-invasive stage. Radical surgical procedures are less apt to meet with success except in the hands of the most skilled surgeons.

Radiation therapy should be carried out by the combined efforts of the radiologist and gynecologist. Approximately 5000 r of combined x-ray and radium are given during a 6-week period. In order to radiate the tumor adequately, the dosage may be such that therapy is carried to the point of a skin blistering reaction. The primary complications encountered are vaginal hemorrhage, vaginal stenosis, rectal ulceration and cystitis. Radiation sickness, if it occurs, usually responds satisfactorily to vitamin B complex.

(The authors' statement that the treatment of choice in small clinics should be irradiation in all cases of cervical cancer except those in the preinvasive stage seems to me to be a very sound one. In the present somewhat transitional stage of this question, and the conflicting statistics which fill the literature, it seems to be true that if one had to depend upon one therapeutic agency, irradiation would be the one selected by most of us. This does not mean that the recent trend to surgery in the early group, or for that matter the extension of very radical surgery to even very advanced cases, is to be criticized, if the still rather experimental nature of these surgical procedures is fully recognized. It is still too early to be sure that even in the hands of expert operators surgery in Stage I cases is going to yield better results than irradiation, and that the salvage or the palliation yielded by the Brunschwig type of operations will justify a continuance of the procedure, even in the few clinics adequately equipped for carrying it out. By and large it would seem that small clinics would be smart to stick for the present to irradiation as the safest routine plan.—Ed.)

HYPERPLASIA AND CANCER

LUCIA TERLÓ

Acta Endocr. et Gynec. Hisp.-Lusitana, 1: 332, 1948

A case is reported in which pathological report revealed cystic endometrial hyperplasia. This condition resisted all conservative therapeutic measures in-

stituted. Hysterectomy was performed and microscopic study disclosed endometrial hyperplasia coexisting with an incipient adenocarcinoma of the uterine body.

The author points out the difficulties arising in the differential diagnosis of patients presenting uterine bleeding, and considers the various therapeutic plans to be followed in cases of metropathia hemorrhagica. He also brings up the question of a probable origin of adenocarcinoma from a hyperplastic endometrium, and considers excessive estrogenic hormone as one of the main causes of endometrial hyperplasia.

(Unfortunately the age of this patient is not given in this abstract, and the original paper is not available for comment. The age factor is of importance, since hyperplasia during the reproductive epoch appears not to predispose in any way to adenocarcinoma, while postmenopausal hyperplasia is not infrequently associated with endometrial carcinoma. On the latter point I personally am quite convinced, on the basis of studies we have made in our own laboratory (Novak and Yui, *Am. J. Obst. & Gynec.* 32: 674, 1936), as well as those of other investigators (Taylor, Breipohl). As a matter of fact, in more than 24 per cent of 104 cases of adenocarcinoma we found a co-existing hyperplasia at some part of the same uterus. In the occasional case it is possible to demonstrate a direct histological transition from frankly benign hyperplasia to atypical proliferative hyperplasia and then to frank adenocarcinoma. The source of the estrogen which produces postmenopausal hyperplasia is believed to be extraovarian, probably in the adrenal cortex, and the role of the estrogen in the production of carcinoma is quite surely only a predisposing one.—Ed.)

UNSUSPECTED ABDOMINAL CHORIONEPITHELIOMA

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Am. J. Obst. & Gynec., 56: 1195-1197, December, 1948

A case is reported of a 27-year-old female who was admitted to the hospital because of a mass in her abdomen. The mass had first been noticed by the patient about 5 months previously. She had also noticed some intermittent vaginal bleeding and an afternoon rise in temperature. A pregnancy had ended in abortion about 7 months prior to her hospital admission. Following the abortion, the menstrual periods were regular until the onset of the more continuous bleeding. On examination, the patient was somewhat underweight. The abdomen showed a large, firm, painless, slightly movable, globular tumor reaching up to the level of the umbilicus. On pelvic examination, the cervix was normal and the uterus was pushed to the left by the mass. The patient was scheduled for operation but developed a cough and fever so that operation was postponed. However, instead of improving, she rapidly developed abdominal pain, tympanism, nausea and vomiting, so that it was felt advisable to do an immediate laparotomy. At operation a large mass looking like an endometrial cyst was found with many smaller pieces of tissue attached to the abdominal organs. The mass arose from the uterus so that a subtotal hysterectomy and bilateral salpingo-oophorectomy were

done. A great deal of bleeding was encountered and postoperatively, despite repeated plasma transfusions, the patient succumbed. Pathological examination showed the mass to be chorionepithelioma.

The author points out that a correct preoperative diagnosis was not made in this case, and he enumerates the pitfalls which were encountered: (1) the size, contour and consistency were not typical; (2) the growth was not associated with the abortion which had occurred 7 months previously; (3) the misinterpretation of uterine bleeding; and (4) the relatively good general condition of the patient despite a rather advanced tumor. 1 figure.

(The author may well be forgiven for not having diagnosed this chorionepithelioma preoperatively, and, in view of the pitfalls in the diagnostic problem as he enumerates them, I doubt whether anyone would have suspected the real condition. Had the bleeding followed the abortion 7 months previously, there might have been more reason for at least suspecting the possibility of chorionepithelioma and trying to fortify the suspicion by biological tests.—Ed.)

CHORIONEPITHELIOMA OF THE UTERINE CERVIX

M. R. ROUCHY

Comptes Rendus de la Soc. Franc. de Gynec. 18: 76, 1948

A 29-year-old multipara female had had a curettage-induced abortion followed by irregular bleeding, which became profuse 3 months later. Pelvic examination disclosed a hemorrhagic tumor on the anterior lip of the cervix, which, on biopsy, proved to be a chorionepithelioma of the mixed variety. Panhysterectomy was performed and pathologic report of the specimen revealed the tumor located in the cervix. A year has already elapsed, and so far patient is in good condition.

(Assuming that the histologic interpretation of this case is correct, it would indeed be a unique one. Since cervical implantation can occur, there would seem to be no reason why a primary cervical chorionepithelioma might not also occur. Without having combed the literature intensively on this point, I do not recall having read of any other report of this situs for primary chorionepithelioma. One must of course think of various other possibilities in connection with such a rare lesion. For example, it would not be so unusual to have local invasion of the vaginal vault and probably the cervix also in association with chorionepithelioma of the uterine body, and quite a number of cases have been reported in which the original chorionepithelioma has undergone complete regression and disappearance but the patient has gone on to die of the metastases. Such a case, with a review of others in the literature, was reported by Novak and Koff in 1930 (*Am. J. Obst. & Gynec.* 20: 153, 1930).—Ed.)

UNUSUAL TYPES OF CHORIONEPITHELIOMA

V. M. DONATO

Bol. de la Soc. de Obst. y Ginec. de Buenos Aires, 27: 176, 1948

Two cases of malignant chorionepithelioma developing after expulsion of hydatidiform mole are presented. In one of the cases, biologic tests (Friedman) were negative, and this fact may be explained by the insensibility of the animal employed in the test, very small nodules showing low proliferative activity, deficient absorption of gonadotrophins due to thickening of the adjacent connective tissue, nuclear necrobiosis, insufficient renal filtering or destruction of the chorionic hormone at the level of the latter. Anyway, chorionepithelioma was diagnosed histologically. This case tends to demonstrate that one cannot solely depend on biological tests in order to establish diagnosis of this malignant tumor. In this point, it should be emphasized that there are clinical signs which may lead to the suspicion of chorionepithelioma: finding of uterine bleeding or of a uterus which continues to grow following delivery, abortion or expulsion of a mole. Bleeding may cease and the uterus may return to its normal size within a few days, followed by recurrence of the same symptoms within an early future. In such an event, the possibility of chorionepithelioma should be borne in mind.

The second case, also quite infrequent, deals with the finding of 2 vaginal tumors which proved to be chorionepithelioma on histologic examination. They are explained by hematogenic transportation of chorionic elements to the vagina.

These unusual forms of chorionepithelioma are likely to constitute diagnostic surprises, and ought to demand from the physician a very careful examination of his patients.

(The author's discussion of the questions suggested by the reported cases is a very intelligent one. It is well known that chorionepithelioma may be present even when biologic tests are not only not high, but completely negative. These negative phases may be only temporary, but in some cases continue for long periods. They can scarcely be explained by the refractoriness of the many animals employed in such long testing periods. Just what the explanation is of the hormone negativity is not known, but it has always seemed to me that a likely explanation is suggested by the characteristically destructive effect of the malignant trophoblastic cells upon surrounding tissues, thus conceivably preventing the ingress of the trophoblastic hormone into the maternal circulation.

The diagnosis of chorionepithelioma is based on the histological examination of the tumor and not on its biological characteristics. In some cases a diagnosis can be made from curettings alone, but unfortunately a good many chorionepitheliomas are intramural and beyond the reach of the curette. Histological diagnosis is possible only after hysterectomy, except in the presence of more accessible metastatic nodules, usually in the vagina. Hysterectomy is therefore necessary in many cases to establish the diagnosis. This does not of course mean that removal of the uterus is indicated in all cases of apparently benign hydatidiform mole, but it does mean that if after a mole is evacuated, with often a second curetting later on, when the uterus is smaller and firmer and thus permits of more complete curettage, and the hormone titer is still high, hysterectomy is indicated, especially if the uterus has remained subinvolved and bleeding has continued. Even under such conditions, a chorionepithelioma will not usually be found. Far more frequently examination of the uterus will show residua

of a histologically benign mole deep in the uterine wall, usually within blood vessels, and obviously beyond the reach of the curette. In a smaller group it will reveal large fields of trophoblast extending from the surface of the villi deep into the uterine musculature and blood vessels, constituting the so-called malignant or destructive mole to which Ewing gave the rather inept designation of chorioadenoma destruens. This lesion, however, is only locally invasive, it does not metastasize like a chorionepithelioma, and it can always be cured by hysterectomy. Unlike some authors, I do not believe it should be spoken of as malignant in spite of its local invasiveness, and in spite of the fact that it can, in rare cases, produce death by either intraabdominal or vaginal hemorrhage. Unfortunately, many of these cases go down in the literature as chorionepithelioma, thus sadly vitiating the statistics of the subject.

In a small proportion of the uteri removed under the circumstances described above, microscopic examination shows a frank chorionepithelioma, the diagnosis of which is usually so clear that experienced pathologists are not likely to differ. The confusion existing in this microscopic field does not come from false positives, but from false negatives, various benign trophoblastic lesions, from simple syncytial endometritis to chorioadenoma destruens, being incorrectly diagnosed as chorionepithelioma. However, it is the occasional existence of a genuine chorionepithelioma, not differentiable from benign trophoblastic lesions by clinical or biological studies, which fully justifies the performance of hysterectomy under such conditions as have been described.—Ed.)

FOUR CASES OF GRANULOMA INGUINALE OF CERVIX DIAGNOSED CLINICALLY AS CARCINOMA

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Am. J. Obst. & Gynec., 56: 1181-1183, December, 1948

In the woman, granuloma inguinale produces an ulcerative lesion which most frequently involves the inguinal region and external genitalia. However, other areas may be involved, and when the cervix is affected it bears a striking resemblance to carcinoma. The diagnosis of granuloma inguinale can be established readily by the discovery of the Donovan bodies in the pathognomonic cells.

Four cases of granuloma inguinale of the cervix are reported by the authors. These cases were similar in that the patients complained of vaginal discharge, irregular bleeding and perhaps lower abdominal pain, while the examination revealed ulcerations of the cervix which bled readily on manipulation. Frequently there was extensive parametrial induration as well; however, examination of the stained material from the edge of the ulceration disclosed the identity of the process.

In all cases where carcinoma is suspected clinically, but is not confirmed by histological study, properly stained material should be examined for the presence of the "granuloma" cell and its Donovan bodies.

(No matter how obvious the diagnosis of carcinoma appears to be on simple clinical examination of a cervical lesion, treatment should always be preceded by histological study

of biopsy material. Usually the diagnosis is confirmed, but occasionally one gets a surprise. In a recent case of our own, and in a number passing through our laboratory in preceding years, tuberculosis was found. Not long ago I was sent sections of a supposedly malignant lesion in the cervix of a pregnant woman. It was a benign condyloma acuminatum, as proved by the subsequent course. Others have reported benign condylomas simulating malignancy, while granuloma inguinale must also be considered among the possibilities, as shown by such reports as that of Speiser and others in the literature.—Ed.)

HISTOLOGICAL BASIS FOR THE TREATMENT OF CHRONIC CERVICITIS

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Brazil

An. Bras. de Gin. 26: 23, 1948

According to the author's opinion, the first step to be taken in the treatment of chronic cervicitis should be to perform a biopsy from the cervical lesion followed by thorough microscopic study of the latter. The histological picture of the lesion will enable one to rule out an otherwise unrecognized carcinoma, aside from obtaining an idea of the extension and type of the inflammatory process present, on which ought to be based the therapeutic plan and technic to be followed.

Based upon the histological study of 40 cases of chronic cervicitis (34 biopsy and 6 surgical specimens), the author presents the following histological grading of chronic cervicitis: *Endocervicitis*—grade I (inflammatory process limited to the endocervical glands with moderate peri-glandular round cell infiltration); grade II (inflammatory process invading the deep cervical parenchyma); grade III (endocervicitis with squamous metaplasia of the endocervical epithelium or atypical endocervical hyperplasia). *Ectocervicitis*—grade I (true erosion or pseudo-erosion with superficial round cell infiltration); grade II (erosion, pseudo-erosion with Nabothian cysts or lacerated and chronically infected cervix with deep round cell infiltration); grade III (chronic infection of the cervix with moderate atypical cornified epithelium with or without proliferation—Hinselmann's groups I and II—or with basal cell hyperactivity of the cervical squamous epithelium). *Ecto-endocervicitis*—grade I (coexistence of endocervicitis I or II and ectocervicitis I or II); grade II (coexistence of endocervicitis I and II and ectocervicitis III, or endocervicitis III with ectocervicitis I and II); grade III (endocervicitis III with ectocervicitis III).

The author advises, based upon this histological gradation, the following therapeutic plan for chronic cervicitis: electro-surgical treatment for endo- or ectocervicitis grade I or II, and for ecto-endocervicitis grade I. The histological grading of cervicitis will indicate, as thoroughly as possible, the technic to be used and the deepness to be reached by the coagulation. Efforts should be made

to accomplish the histological cure of the case and, at the same time, avoid too radical a destruction of tissues which may cause numerous complications (hemorrhages, stenosis, sterility, dysmenorrhea, difficult low deliveries).

For endo or ectocervicitis grade III and ecto-endocervicitis grade II or III, treatment ought to be surgical, consisting of the removal of the cervix (Sturmdorf conization, high flat amputation of the cervix) or of the polypoid hyperplasia, thus permitting the removal of all suspicious areas. This undoubtedly constitutes a decisive step for the complete cure of the patient besides permitting a thorough microscopic study of the whole cervix, a detail which should never be neglected in such cases.

(This impresses me as a very good paper, especially from the standpoint of the histological study of the varying degrees and types of lesions which are so commonly lumped together under the designation of cervicitis. The chief groups differentiated by the author—endocervicitis, ectocervicitis and ecto-endocervicitis—are the fundamental ones, and they can often be differentiated clinically by careful inspection of the cervix. On the other hand, it seems to me that the sub-varieties which he describes are less important as a guide to treatment. This would apply especially to the intracervical group, which are not nearly as accessible to biopsy study as the ectocervical variety, even were biopsy studies considered routinely advisable before resorting to treatment.

The author is on safe grounds, however, in stressing that the plan of treatment should be adapted to the type of chronic cervicitis which exists. For example, the cervix which is moderately hypertrophied and which presents a large granular erosion surrounding the canal, can often be restored to a practically normal appearance through a properly performed simple radial electrocauterization. On the other hand, one frequently sees cervixes which present a normal-appearing external surface, but which show great quantities of thick mucopurulent exudate from within the canal. Cauterization in such cases would be highly illogical and certainly unsuccessful, aside from such hazards as that of producing strictures of the cervical os, especially when the latter is of small calibre, as is so often the case. The therapeutic approach to such cases must envisage the removal of the infected endocervix by some such procedure as conization, Sturmdorf tracheloplasty, or trachelectomy, depending upon such factors as the age and reproductive status of the patient as well as the personal predilection of the individual gynecologist.

The fundamental thesis of the author, therefore, is a sound one, i.e. that chronic infection of the cervix can not be treated by rule of thumb, but that here, as in every other therapeutic problem, individualization must be the keynote.—Ed.)

RUPTURED HORN OF A BICORNATE UTERUS

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J. Obst. & Gynec. Brit. Emp., 55: 501, August, 1948

The case is presented of a 24-year-old white female who gave a history of painful menstruation from the age of the appearance of the menses until she conceived. After conception she had slight spotting of blood on several occasions and it was thought that perhaps her pregnancy was complicated by a fibroid.

At the 18th week of pregnancy she was seized with a severe pain in the left side of the abdomen and this was followed by vaginal bleeding. A state of shock developed and the abdomen was distended, rigid and tender. A laparotomy was performed as soon as blood was obtained for transfusions. The fetus within its sac was lying free in the peritoneal cavity which also contained a large amount of free blood. One horn of a bicornate uterus was ruptured across its fundus. This horn was removed. The other horn, which was well developed, and both Fallopian tubes and ovaries were conserved. The patient made a rapid recovery which was complicated only by a persistent urinary infection. A uterine cast was passed in 2 pieces during the first week after pregnancy. Afterward, the patient had no further dysmenorrhea and hysterosalpingography confirmed that the remaining horn was well developed and of good shape. The management and outcome of subsequent pregnancies were questioned.

(While ectopic pregnancy in a rudimentary horn is far less common than the ordinary tubal pregnancy, it is apt, like the rare interstitial tubal variety, to be associated with more profuse intraabdominal hemorrhage. Moreover, the diagnostic problem before rupture may be a more difficult one, since the pregnant rudimentary horn forms a part of the uterus, producing an asymmetrical enlargement of the cornual region which is easily mistaken for a myoma. The history and pelvic findings thus often simulate a threatened early abortion, and this incorrect diagnosis is often made until the rupture takes place.

It is of interest to note that this patient had always had dysmenorrhea before the operation but that following the latter there was no menstrual pain. This indicates the importance of rudimentary cornua as a rare but possible cause of what is likely to be considered primary dysmenorrhea. The mechanism in these cases appears to be an excitation of colicky muscular contractions by the menstrual blood accumulating within the small cornual cavity, which often has only slight or possibly no communication with the cavity of the uterus proper.—Ed.)

HETEROLOGOUS TUMOR OF THE CERVIX UTERI

V. M. DONATO, J. GONZALEZ AND J. M. LASCANO

Bol. de la Soc. de Obst. y Ginec. de Buenos Aires, 27: 40, 1948

A cervical polyp was removed from a patient, with recurrence 5 months later. It was removed again and 2 months thereafter a second recurrence was noticed. At this time, however, the gross aspect of the polyp resembled very closely the vesicles of hydatidiform mole. In view of such findings, panhysterectomy was performed and pathologic examination revealed neoplastic masses showing areas with typical sarcomatous changes.

A comment is made on these infrequent heterologous types of tumor of the corpus and cervix uteri, which should always require radical surgical treatment followed by radiotherapy.

The authors arrive at the following conclusions: 1) Every removed polyp should be carefully studied histologically; 2) polyps which prove to be histologically

benign should demand periodic check-ups of the patient; 3) every recurrence occurring within a short period of time ought to be considered as of sarcomatous character, and treatment should follow along these lines; 4) an identical therapeutic plan should be followed in cases of acini polyps of the myxomatous type.

One should always bear in mind the fact that apparently benign polyps protruding from the cervical canal may occasionally be responsible for the overlooking of heterologous structures with extreme malignant propensities.

(This was evidently a case of sarcoma botryoides, the grape-like sarcoma which so often contains mixed mesodermal elements especially, and rather curiously striped muscle tissue. There would seem to be little doubt as to the kinship of this group with the mixed mesodermal tumors of the uterine body, though these also are rare. The authors wisely call attention to the importance of histological examination of every polyp, either of cervical or endometrial origin. Sarcomas of the endometrium and endocervix have a characteristic tendency to become polypoid, although the polyps which may protrude from the cervix are likely to be of bulkier and more infiltrated type than the usually fragile and soft cervical polyps of benign character.—Ed.)

INFARCTION OF THE UTERUS

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J. Obst. & Gynaec. Brit. Emp., 55: 513-514, August, 1948

The uterus, without doubt, has one of the best vascular supplies of any organ in the body and therefore infarction is very rare. The word infarct usually implies a localized area of necrosis resulting from cutting off of the blood supply to the particular area. However, it is also applicable when a widespread necrosis is due to multiple small thrombi, often visible only through the microscope. The author describes 4 cases of both types, each one having a different etiology.

The first patient was a 21-year-old female who was almost moribund and with gangrene of both feet. By error, this patient had received one ounce of liquid extract of ergot twice daily for 3 weeks. At autopsy there was generalized contraction of the blood vessels and multiple infarcts throughout the body. The uterus was completely involuted; all 4 main vessels contained organized thrombi and the uterus itself was turned into a solid infarct which, on section, was structureless.

The second case concerned a woman of 58 years who complained of acute abdominal pain and vomiting of 12 hours' duration. At operation she was found to have a uterine fibroid which, on account of gross elongation and atrophy of the supravaginal cervix, had caused axial rotation of the corpus through more than a complete circle, carrying with it both ovaries. All 4 main vessels showed thrombi and the uterus was plum-colored and necrotic. The woman recovered after hysterectomy.

The third patient was a 35-year-old white woman, admitted to the hospital at the 14th week of pregnancy with a threatened abortion. There was slight vaginal bleeding and the blood pressure was 180/120. Ten hours after admission she complained of a sudden abdominal pain, collapsed and died, all in the space of 10 minutes. At autopsy she was found to have extensive atheroma, and there was an infarct of the left ovary and left cornu of the uterus. A fresh thrombus was found in the left ovarian artery which had extended to involve many of the small ramifications of the vessels, thereby preventing the formation of a collateral circulation.

The fourth case was that of a 58-year-old woman who complained of vaginal hemorrhage. At examination the cervix appeared gangrenous and section showed thrombosis of the small vessels and extensive septic infarcts. It was learned that she had tried to remove a prolapse by cutting it off with a pair of scissors. She developed pain in the left iliac fossa, and at operation a large vessel at the left cornu was thrombosed with infarction at that portion of the uterus. The patient recovered after hysterectomy.

Thus, 4 ways in which thrombi may be formed are presented: a chemical agent, mechanical obstruction, vascular disease and a septic process. Total infarction of the uterus is extremely rare and the power of the uterus to recover from anything short of total vascular occlusion is good.

(The finding of thrombi in the uterine veins in association with necrosis would scarcely justify the designation of infarct, as this term is ordinarily employed by pathologists, although such factors as axial rotation of the uterus or septic infection can no doubt produce profound circulatory disturbance. It is difficult to believe that a local accident such as the "infarct" of the left ovary and left uterine cornu could bring about almost instant death, though the occurrence of severe pain would be understandable enough. The collateral circulation in the uterus is so good that, as the author himself says, it would be expected to recover from "anything short of total vascular occlusion". All in all, it would seem to me that a good case has not been made out for uterine infarction as a clinical entity.—Ed.)

ABNORMAL UTERINE BLEEDING

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Mississippi Doctor, 26: 146-151, November, 1948

In the interest of brevity, the causes of abnormal uterine bleeding may be classified as follows: (1) complications of pregnancy; (2) systemic diseases; (3) organic lesions of the reproductive tract; and (4) functional uterine bleeding.

Millen and Shepard found that 21 per cent of cases of premenopausal bleeding were due to complications of pregnancy. The most common complication encountered during pregnancy is abortion. Ectopic pregnancy usually causes abnormal uterine bleeding, Hagood and Otts finding that 83.3 per cent of such

cases exhibited vaginal bleeding as a symptom. Both hydatidiform mole and chorionepithelioma cause abnormal uterine bleeding. In chorionepithelioma, further bleeding after curettage is almost pathognomonic. Subinvolution of the uterus and placental site bleeding are further causes of abnormal uterine bleeding as a result of pregnancy complications.

Accumulating data indicate that uterine bleeding can derive from systemic as well as purely local disturbances. The systemic diseases most commonly associated with abnormal uterine bleeding are diabetes, mumps-oophoritis, malaria, typhoid fever, tuberculosis, syphilis and the blood dyscrasias. The author cites 3 cases of abnormal bleeding due to systemic disease that he has seen during the past 2 years. One case was due to syphilis, and after treatment with penicillin, the patient has had regular normal periods, with no abnormalities disclosed on pelvic examination. The second case of abnormal uterine bleeding was due to acute myelogenous leukemia. This disease caused her death 6 months later. She undoubtedly had a fibroid, but the leukemia caused her death and perhaps her bleeding. The third patient suffered from telangiectasia. From the onset of her menses she had always bled profusely and passed many clots. Menopause was artificially induced at the age of 47.

Among organic lesions in the reproductive tract causing abnormal uterine bleeding, malignant disease is by far the most serious. However, organic lesions may exist at any age. During the prepubital ages, ovarian tumor and vulvovaginitis should be considered. In the second decade of life, the most common causes of abnormal bleeding are endocrine disturbances and inflammation. Millen and Shepard found that the commonest causes of abnormal bleeding during the reproductive age were complications of pregnancy, pelvic inflammatory disease, and fibroids alone or fibroids in association with adenomyoma, ovarian tumors and polypi of the cervix and uterus. The cause of bleeding after the menopause is cancer in approximately 50 per cent of cases. The danger of treating menopausal patients with endocrine therapy without a thorough examination is stressed. In summary, the proper early diagnosis of the cause of the bleeding is the important feature; treatment is fairly standard and well known for the different lesions.

Functional uterine bleeding, or bleeding for which no pathological cause can be found, occurs most frequently at the beginning or end of reproductive life. Bleeding at puberty is usually due to failure of ovulation, estrogen being secreted by follicular cysts, and hyperplasia of the endometrium resulting from the excessive estrogen secretion. The endometrial pattern is of the Swiss cheese type. The same derangement in physiology explains functional bleeding at the menopause, the ovaries becoming refractory to pituitary stimulation, and atretic follicles and cysts forming to cause the prolonged estrogenic stimulation of the endometrium.

Ovulation bleeding is quite common. The author has observed a 24-year-old patient who has a 3-day "period" 10 days after the start of her normal period. Temperature graphs show that she is ovulating during this short bleeding phase.

Bleeding that occurs from secretory endometrium is termed "irregular shed-

ding." This disorder is characterized by the prolongation of the desquamation phase of the menstrual cycle. This type of bleeding is not clearly understood, though it is thought to be due to some variation in progesterone stimulation.

In managing cases of functional uterine bleeding, it should be remembered that in a great many instances the condition is self-limited, and spontaneous cures may be expected in a large percentage of cases. There is no specific therapy, but the following measures are currently in use:

1. Diet rich in proteins, vitamin C and K, calcium and iron.
2. Specific endocrine therapy has included practically all the known hormones. At most, endocrine therapy is substitution therapy, and it may be surmised that many of the cures credited to endocrine therapy are in reality spontaneous cures. Estrogen and progesterone, given to stimulate normal ovarian function, appear to be on a more rational basis than administration of gonadotrophins and androgens.
3. Snake venom, with action on the blood vessels similar to that of ergotrate preparations, has been suggested.
4. Curettage is the most useful procedure in the management of functional uterine bleeding, and the additional knowledge derived from study of the endometrial scrapings is valuable. Curettage should be employed before any treatment with endocrine preparations is instituted, particularly in the menopausal age group.
5. Radium therapy in the menopausal age group is favored by some gynecologists.
6. Hysterectomy is a last resort.

(A short but sensible résumé of a big subject, which should be of value to the general practitioners for whom it is primarily intended.—Ed.)

THE ADNEXA

THE BACTERIOLOGY OF FALLOPIAN TUBES REMOVED AT OPERATION

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Am. J. Obst. & Gynec., 56: 1142-1145, December, 1948

This investigation comprises a study of 72 patients from both the wards and private service of the Women's Clinic of Johns Hopkins Hospital. Seven patients had a previous history of gonorrheal infection, 40 had doubtful histories and 25 had negative histories. Immediately upon removal of the infected tubes at operation the material was cultured aerobically and anaerobically on a variety of media.

In this study it was not possible to isolate the gonococcus from the Fallopian tubes showing histological evidence of subacute and chronic inflammation, so that it was felt that the tubes were not a focus of chronic gonorrheal infection. The gonococcus is short lived in the tubal mucosa and apparently produces a low level of demonstrable antibodies, as only 2 patients had positive gonococcus complement fixation tests. Two of the cases were of special interest in that the predominating organism in the abscesses was *actinomyces muris* in one case and *hemophilus influenzae* in the other. Pus producing organisms were isolated in 13.8 per cent of the cases with the staphylococcus and streptococcus being the most common offenders.

(Since the original work of Curtis, indicating the comparatively short survival of the gonococcus in the tubes, there has been some fluctuation of opinion on this point, but the studies of Koch appear to bear out Curtis' viewpoint.—Ed.)

PRECOCIOUS PUBERTY IN A THREE YEAR OLD GIRL

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Illinois M. J., 94: 322-324, November, 1948

The case is presented of a 3-year-old girl who exhibited symptoms of precocious puberty and an enlargement of the abdomen, somewhat greater in the right lower quadrant. The child was bright, with normal gait and clear, rapid speech. Her parents stated that a while after birth she had exhibited a prepuberal state, characterized by fat accumulation, particularly in the breasts. Two months

before the present examination her breasts had again increased in size and irregular menstruation took place. The child was fond of using nail polish and lipstick, and frequently asked her father to caress her breasts. This reaction suggests the establishment of erotogenic zones in the breasts related to a definite sexual desire corresponding to a precocious libido. A pelvic-abdominal tumor was observed which projected into the right lower quadrant. There was no pubic or axillary hair.

A conservative operation was performed, a tumor being found and removed together with the right tube and ovary. The pathological report classified the tumor as a granulosa cell tumor, typical in some areas, atypical in others because of extensive cystic degeneration of the epithelial nests.

Two months after operation breast hypertrophy had diminished, there was no more menstruation and her psyche was that of an infant. Prognosis is doubtful because these tumors sometimes recur. 4 figures.

(Through the kindness of Dr. Sarrelangue I had the opportunity of examining sections of the ovarian tumor in this case, and there is no question as to its proper classification as a granulosa cell tumor. The history, too, was quite typical, showing the syndrome of precocious puberty plus the presence of a definite ovarian tumor. The latter point may be stressed, chiefly because the gynecologist, knowing that granulosa cell tumors in children produce precocious puberty, may wrongly assume, when confronted with a case of the latter, that a tumor must be present somewhere in the ovaries even though none can be palpated. Exploratory operations have often been done on this wrong assumption. It should be remembered that far more frequently precocious puberty is of the so-called constitutional type, in which an otherwise perfectly normal puberty mechanism is for some unknown reason inaugurated at an abnormally early age. In these cases there is no demonstrable tumor of the ovaries or of any other endocrine gland. I have reported a considerable group of such cases (*Am. J. Obst. & Gynec.* 47: 20, 1944) and have had the opportunity of re-examining and tracing some of these patients for many years. One of these, whom I saw at the age of 6, was recently, some 14 years later, married and has passed through a normal full term pregnancy.

The ovaries of children with the constitutional type of precocious puberty are of post-puberal type, and such youngsters exhibit not only precocious menstruation but also precocious ovulation so that they can conceive if inseminated. It is in this group that there occur the remarkable cases of abnormally early motherhood, the youngest on record being Lina Medina, the Peruvian child who was delivered by cesarean section at full term at the age of 5 years and 8 months.

On the other hand, the much less common cases of precocious puberty due to granulosa cell tumor have menstrual, or perhaps better, pseudomenstrual bleeding, but do not ovulate, the bleeding being of purely estrogen-induced type. Such patients cannot of course conceive. The practical point in treatment is that if the ovaries are of entirely normal size in a case of precocious puberty, there is no indication for operation. If one of the ovaries shows definite enlargement, an operation is usually justified, but even then a tumor is not always found, as the enlargement may be due to a small follicular cyst.

There are of course still other types of precocious puberty, such as those due to adrenal neoplasms or lesions of the midbrain, the latter probably including the pineal gland cases, though this variety seems to occur only in males. The adrenal cases can often be segregated fairly well on clinical grounds, since the premature development is of heterosexual type, including usually marked hypertrophy of the clitoris, while only in a small proportion is precocious menstruation a part of the syndrome.—Ed.)

THE SIGNIFICANCE OF CYSTIC ENLARGEMENT OF THE OVARY
WITH RESPECT TO TREATMENT

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Normal ovarian function entails the formation and rupture of a cyst, the graafian follicle. Any interruption or perversion of the normal course of events may give rise to oversized follicles or enlarged corpora lutea containing fluid. These are the non-neoplastic or physiologic cysts. The management of such cysts involves their differentiation from cystomas, and treatment where necessary is to remove etiologic factors and to offset symptoms. Gross and histologic examination of these non-neoplastic cysts is discussed.

Acute bacterial inflammation in the pelvic organs may give rise to diffuse oophoritis, with thickening of the ovarian capsule and adhesion to surrounding structures. Local mechanical factors may have an important role in cystic formation. Ovarian prolapse with passive congestion and edema can result in cellular embarrassment and alter the pattern of the graafian follicle growth.

Alteration of the hormonal stimuli, as well as changes in ovarian responsiveness, can be the source of cystosis. The influence that arrests the development of follicles and causes their degeneration is unknown. The absence of such a principle would account for the persistence of a follicle. Rapid growth of oversized follicles occurs following the release of large quantities of chorionic gonadotropin. Whatever the initial hormonal imbalance, ovarian cysts lined with granulosa or theca lutein cells are the outcome. The cause for the persistence of a corpus luteum cyst is obscure.

Clinical differentiation of the non-neoplastic cyst from a true cystoma is difficult, but the presumptive evidence is adequate. The probability of a physiologic origin in a small ovarian cyst is overwhelming, and the risk in delay in the treatment of an ovarian malignancy is small. A few weeks of careful observation are better than wholesale laparotomy.

Symptoms can arise from local organic changes in the ovary or altered hormonal production. Bilateral, deep and boring pain can arise from increased intracapsular ovarian pressure and congestion. Mild degrees of menorrhagia may be encountered. A persistence of corpus luteum can cause abrupt amenorrhea. Various other non-specific symptoms may be present; but many cysts are asymptomatic. The role of the simple retention cyst is trivial and transient. The symptoms are likely to disappear without any treatment. Vigorous treatment of a cystosis is reasonable only when the associated manifestation is chronic and disabling.

In the vast majority of cases simple repeated examination to rule out the possibility of a cystoma is the only treatment necessary. Correction of uterine displacement and control of pelvic inflammation are sometimes useful therapy.

Hormonal therapy is largely empiric. Gonadotropic extracts are probably worthless. Large doses of stilbestrol may reduce the incidence of ovarian cystosis and testosterone may retard cyst development.

Surgical interference with a process whose origins are only partly local, and in which the lesion is apt to disappear without treatment, is of questionable value. The indications or possible advantages of presacral neurectomy, oophorectomy and partial resection of the ovary are discussed. However, the author emphasizes surgical restraint at all times. 6 figures.

(The cystic ovary, which took such a beating in an earlier generation of gynecology, and which is still far from safe from surgical attack, is almost always a pretty inoffensive structure, and doesn't deserve the persecution to which it has been subjected. Various conditions are included under this designation, as the author points out. The cystic ovaries often found with marked chronic inflammatory disease show many small cystic cavities which are simply blighted or atretic follicles. On the other hand, in certain cases of functional bleeding of anovulatory type, there are many tiny cystic follicles which are lined by a well-preserved granulosa and which still are actively functional, producing excessive amounts of estrogen. In other cases of the same functional disorder, one ovary may contain a follicular cyst a good many centimeters in diameter, a persistent cystic but actively functioning follicle, in contrast to the more common follicular cyst which is a cystic atretic follicle without estrogenic function. Again, the marked cystic changes often seen in conserved fragments of ovarian tissue are probably less frequently due to circulatory disturbance than to the continued stimulation by the pituitary gonadotrophic hormones of a reduced ovarian surface.

Still other types of non-neoplastic cystic ovaries might be described, such as those which are often seen in association with hydatidiform mole or chorionepithelioma, in which case the cyst wall shows luteinized thecal or granulosa cells.

The author wisely cautions against operating upon small cysts of the ovary, since the majority of these are non-neoplastic and transitory. A cyst as large as a lemon at one examination may have completely involuted at a subsequent examination a month later, for this is the tendency of retention cysts of this type. In this respect such cysts are similar to benign breast cysts, which not infrequently disappear as quickly as they appear, though there are exceptions. A reasonable period of observation should be the rule with the smaller cysts of the ovary, and this subjects the patient to no hazard. If, instead of regressing, the cyst becomes steadily larger and larger, it may be assumed that it is of genuinely neoplastic, probably cystadenomatous type, and operation is advisable.—Ed.)

BILATERAL OVARIAN FIBROMA

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Am. J. Obst. & Gynec., 56: 1188-1191, December, 1948

The case is reported of a 73-year-old white female who was admitted to the hospital with complaints of pain and masses in the abdomen and loss of weight and strength. The masses had become progressively larger over a 2-year period.

Menstruation had been normal and the menopause occurred at the age of 45 years. On examination, 3 masses were felt, the 2 lateral masses being about the size of a grapefruit and the central mass over the symphysis being somewhat smaller. The masses were also felt on pelvic examination but the one on the right did not seem to be connected to the adnexa. The remainder of the physical examination and laboratory studies were not contributory. A laparotomy was performed and both ovaries were found to be replaced by large, firm nodular tumors. A bilateral salpingo-oophorectomy was performed and the patient made an uneventful recovery. Six months later she was still well.

The cut surface of the tumors was uniform gray-white with a delicate fibrillar pattern and there was some gross lobulation. In one of the tumors there were several cystic areas which contained a thick clear or hemorrhagic fluid. Microscopic examination disclosed round or elongated nuclei within a fibrillar ground substance in an interlacing arrangement closely resembling ovarian stroma. Other areas showed a more loose texture with cells having a vesicular nucleus and stellate cytoplasm. There was some hyaline degeneration and here and there were apparent remains of corpora albicantia. 3 figures.

(While fibromas of the ovary are usually unilateral, there is no reason why, probably as a matter of coincidence rather than as indicative of any especial neoplastic tendency of the particular woman's ovarian tissue, they might not at times be bilateral. I have seen a number of instances of small fibromas which were bilateral. The large tumors described in this patient of 73 had probably developed many years previously, as fibroma is generally a slow-growing tumor.—Ed.)

A VARIANT OF MEIG'S SYNDROME

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J. Obst. & Gynaec. Brit. Emp., 55: 509-510, August, 1948

The patient, a 5-para, aged 61 years, had menstruated regularly until 2 months before admission. In 1941 she first noticed swelling of her abdomen and a paracentesis was carried out. This procedure was repeated 17 times between 1941 and 1943, and during this period she showed gradual though progressive loss of weight. When examined in 1943 she was found to have ascites and a large solid tumor in the right half of the lower abdomen. She also had a bilateral hydrothorax. At laparotomy there were two tumors on the right side of the pelvis. One was cystic and had the fimbriated end of the Fallopian tube stretched over it; this proved to be an ovarian cyst with intracystic papillae. The second tumor mass was solid and arose from the round ligament, lying extraperitoneally. Both of the tumors were removed without difficulty, and chest x-ray 2 weeks later showed complete disappearance of the pleural effusion. Histological examination

of the solid tumor showed it to be a well differentiated adenocarcinoma. The patient made a good recovery and is well 5 years after the operation.

The author points out several interesting features of this case. Solid ovarian tumors which are associated with fluid in the abdomen and chest are often relatively benign but every such case should have an exploratory laparotomy if feasible. There was no obvious explanation why this patient continued to menstruate until the age of 61. The case was also unique in so far as it is the only recorded case of an extraperitoneal tumor causing the syndrome.

(The author speaks of this case as representing a variant of Meigs' syndrome because the fibroma of the round ligament was extraperitoneal. If this were the only tumor present, this viewpoint might be accepted. However, there was another and larger intraperitoneal tumor present in the form of a solid adenocarcinoma, and it is likely that it was this which was responsible for the ascites and hydrothorax. Not only fibroma of the ovary, but various other solid tumors of the ovary, both benign and malignant (Brenner tumor, granulosa cell cancer, thecoma, papillary cancer), have been found in association with Meigs' syndrome. —Ed.)

THE MECHANISM OF METRORRHAGIAS COEXISTING WITH TUMORS OF THE OVARY. PRACTICAL DEDUCTIONS

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Rev. Franç. de Gynéc. et d'Obst. 43: 85, 1948

As a symptom of ovarian tumors, metrorrhagia may be due to either one of the following causes: implantation of the tumor in the body of the uterus, endocrine activity exerted by the tumor upon the uterus, coexistence of uterine and ovarian neoplasms, and finally, a reflex activity originating in the ovarian neoplastic growth itself. The author briefly discusses these various possibilities on the ground of some personal clinical observations. In the case of functioning ovarian tumors with production of endometrial hyperplasia, the author points out the possibility for the latter lesion being surpassed, with the development of cancer as a result. The reactional uterine proliferation accompanying the so-called folliculomas should always be regarded as suspicious. Hence, when an ovarian tumor is encountered associated with metrorrhagia, the surgeon should give preference for the abdominal route, and perform a pan-hysterectomy with excision of the opposite ovary, even though the latter looks grossly normal. If the tumor is associated with cancer, the Wertheim type of operation should constitute the treatment of choice. When an ovarian cyst is encountered, the latter ought to be opened before one decides as to the type of operation to be performed. On the other hand, when abundant ascites is present, subtotal hysterectomy should replace pan-hysterectomy in view of the defective qualities acquired by the peritoneum when exposed in an ascitic milieu.

(The causes of metrorrhagia as a symptom of ovarian tumors are sensibly discussed by the author, except for the vagueness of the last one enumerated, "the reflex activity originating in the growth itself." The author wisely points out that the postmenopausal bleeding produced by granulosa cell tumors and thecomas may be due to the estrogen secreted by the tumor and be associated with simple benign endometrial hyperplasia, but that on the other hand such tumors may incite the development of genuine adenocarcinoma of the endometrium, as has been observed in a considerable group of reported cases. He is also wise in his preference of the abdominal route for ovarian tumors in general, and for complete removal of the pelvic organs when there is any suspicion of malignancy, as there is in almost all cases of solid or semi-solid tumors in older women. His advice to open ovarian cysts as soon as they are removed, before the abdomen is closed, is likewise sound. The gross appearance of the opened tumor will often save the surgeon the humiliation and distress of doing a conservative operation and being told a few days later that the tumor is malignant. On the other hand, I am not sure that I would agree that the presence of ascites should lead the surgeon to do subtotal rather than total hysterectomy. His reason for this is apparently the fear of infection of a peritoneum whose resistance is below normal, but this will not be accepted by all surgeons, nor will the hazard of the total operation seem any greater than with the subtotal. It is probably true that with many ovarian malignancies the retention of the cervix would be associated with minimal risk of cervical recurrence, but there would certainly be a definite hazard in the very group which the author chiefly stresses, those in which adenocarcinoma of the uterus is present in association with the ovarian cancer.—Ed.)

PNEUMO-PYOSALPINX

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J. Obst. & Gynaec. Brit. Emp., 55: 455-458, August, 1948

A nullipara, aged 32 years, was admitted to the hospital complaining of severe lower abdominal pain of 24 hours' duration. Two years previously she had been operated for acute appendicitis, and an appendiceal abscess was found and drained. Following this operation she had had amenorrhea for 6 months and then her periods recurred at 2 to 3-month intervals. On admission her temperature was 102 degrees F., pulse 116 and the blood pressure 120/80. The abdomen was distended below the umbilicus and resonant to percussion. There was exquisite tenderness over the lower abdomen, especially on the right side. Vaginal examination showed marked tenderness of the right anterior and posterior fornices, and there was a profuse greenish, blood-tinged discharge. *Staphylococcus albus* and *fecalis* were grown from the pus. Pus was aspirated from a needle inserted through the posterior fornix. A laparotomy was performed and a gas and fluid filled cyst, measuring 6 inches in diameter, was found in the lower right quadrant. At one point it was firmly adherent to the adjacent bowel. The tumor was ruptured during removal. Postoperatively the patient was given large doses of antibiotic drugs and, except for the formation of a sinus tract, had an uncomplicated recovery. No gas forming bacilli were found in the pus from the

cyst and no fistulous tracts could be discovered by barium enema. Pathological examination showed this cyst to be a dilated and chronically inflamed Fallopian tube.

The presence of the gas in the tumor mass is difficult to explain. Three possible causes are discussed by the author but there is no certainty as to whether any of these was the etiologic agent. The gas might have been accidentally introduced at the time of aspiration. It may have been formed by gas producing bacilli, or, thirdly, there may have been an unrecognized salpingo-intestinal fistula. Though the latter was not demonstrated, it was felt to be the most likely explanation. 2 figures.

(Whatever the explanation of the pneumopyosalpinx in this case may have been, and that suggested by the authors seems as rational as any, the case emphasizes the frequency with which the ubiquitous appendix intrudes into gynecological problems. It is not rare to find that an abscess supposedly of pelvic inflammatory origin proves to be due to a perforated appendix. The moral is that the gynecologist who has had little or no training in general abdominal surgery is likely to handle such cases very poorly. He will be equally at a loss if a left-sided supposedly adnexal mass proves to be an unsuspected sigmoiditis or a carcinoma, or if in a difficult pelvic inflammatory case, he inadvertently tears the intestine so irretrievably as to require an anastomosis. He may not have at his elbow a trained abdominal surgeon who can take over, and the patient is therefore penalized for the gynecologist's unpreparedness to handle such situations. And they are not rare, as every experienced gynecologist knows.

I stress this point, as I have on several previous occasions in these pages, because I believe that many otherwise excellent combined residencies in obstetrics and gynecology include little or no training in the general surgical problems of the abdominal viscera. Gynecology and obstetrics are now happily married, to the advantage of both. Whatever a man later practices, and whichever of the two he accents or excludes, his fundamental training should be in both. There are some, however, who have carried this viewpoint to an extreme, appearing almost to feel that a gynecologist disgraces himself if he is also able to resect the intestine very competently, or to take out an appendix or a gallbladder as expertly as his general surgeon colleague. The pelvis can not be considered a sharply demarcated surgical zone in itself, for it is only a segment of the general abdominal cavity. To say this is far from an endorsement of the view formerly pressed, especially by general surgeons, that gynecology should be considered only a subdivision of general surgery. There is no need at this date to argue the fallacy of such a concept, and the separateness of gynecology as a specialty has long since been assured by its union with obstetrics. When a man marries, his wife has a right to expect him to cut himself off from corrupting associates who would endanger the happiness and success of the marriage, but not from the few who could contribute to making the union a model one.—Ed.)

FEMALE UROLOGY

URETHRAL DIVERTICULUM IN THE FEMALE: A CLINICAL STUDY

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Am. J. Obst. & Gynec., 57: 231-236, November, 1948

The findings in 71 cases of diverticulum of the female urethra in which surgical treatment was employed are presented. This is not an extremely rare lesion, but has received little attention recently, except in a few textbooks.

After dissecting out a good number of these diverticula, the author believes that they originate as congenital defects of the urethra and are subsequently influenced by trauma and non-specific infections. Any diverticulum that cannot empty itself will become infected and produce an abscess.

Diverticula of the urethra never contain all the normal layers of the urethra. Some are of large size and yet there is no history of an abscess in the region.

Furthermore, the author cannot agree with the usual theory concerning diverticula because he is inclined to agree with Cabot that the urethra is devoid of glands except Skene's glands at the external meatus. Infection and trauma are the most common exciting etiologic factors in the production of symptoms.

The cardinal symptoms found in the series of cases studied are discussed. Pain was of 4 types: suprapubic, as in a cystitis; perineal; vaginal and darting pain, from urethra to vagina to pelvic organs.

Leakage of urine was noted in 40 per cent of the cases. The characteristic leakage is that which immediately follows urination.

Dyspareunia was experienced by 10 per cent of the patients, especially those who had acute inflammatory reactions in the anterior vaginal wall.

A mass in the vaginal wall was noted in 40 per cent of the patients. The mass may contain urine, pus or multiple calculi.

The severity of the complaint is out of all proportion to that which physical findings indicate. The duration of the complaint is often significant.

Vaginal examination may reveal some induration or a definite mass. Pressure on the mass may cause foul smelling urine or pus to exude from the urethra. Cystoscopy is not always successful in identifying the diverticulum. If the opening is not occluded it is usually in the midline of the middle third of the urethra. When the orifice can be identified, a small lead catheter should be coiled in the diverticulum and a roentgenogram taken.

The author finds that any local treatment is of no value when a real diverticulum exists. Transurethral incision of a small diverticulum for adequate drainage may be helpful. The best treatment is complete surgical excision of the diverticulum and repair of the urethra.

A retention catheter, No. 18 to 22, should be placed in the urethra so that

the identity of lumen of the urethra is always known. Other helpful points in the surgical technique are discussed.

A catheter is maintained in the urethra for 4 or 5 days; the patient is then advised to go to the bathroom and void. Subsequent catheterizations are inadvisable.

(This paper, written by an operator of large experience and based on a large group of cases of a relatively uncommon lesion, is a valuable one. It is full of practical points as to the management of this troublesome lesion. A good many of these patients come under observation with a history of one or several previous operations, often simple incisions for a supposed "suburethral abscess," at other times after incomplete excision of the diverticulum. While the opening of the urethra entailed by complete dissection of the diverticulum can be closed very readily, the preliminary insertion into the urethra of a sound or catheter is very helpful in avoiding more extensive trauma of the urethral floor. A retention catheter, as Counsellor advises, is almost indispensable to ensure good urethral healing. On one point I believe that many will disagree with the author, and that is his belief that the urethra "is devoid of glands except Skenes' glands at the external meatus." This, it seems to me, has been pretty well disproved by the excellent studies of J. W. Huffman, demonstrating the often intricate pattern of the paraurethral duct system in the female (*Am. J. Obst. & Gynec.* 55:86, 1948—see editorial comment in the *Survey* 3:435, June, 1948).—Ed.)

OPERATIVE GYNECOLOGY

A STATISTICAL REPORT OF 1771 CASES OF HYSTERECTOMY

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Am. J. Obst. & Gynec., 56: 1151-1155, December, 1948

Of the 1771 cases of hysterectomy reviewed in this paper, 71 per cent of the patients had a panhysterectomy and 29 per cent had either a supravaginal or a vaginal hysterectomy. Sixty-eight per cent of the patients were para one plus. The age distribution showed the highest incidence between 30 and 50 years of age, with 80.4 per cent of the patients falling in this age group. Myoma, relaxed vaginal outlet, salpingitis, prolapse and endometriosis were the most common indications in the order named. The most common symptoms were pain, bleeding, tumor mass and prolapse. Numerous additional operative procedures were done at the time of hysterectomy. Appendectomy and perineorrhaphy were frequently done in conjunction with the major procedure, and colporrhaphy and partial or complete removal of the adnexa also often accompanied the hysterectomy. The most common operative complications were injured ureter, torn bladder or torn bowel. Such complications occurred in 1.6 per cent of the cases. The most frequently occurring postoperative complications were infected wounds, cystitis, pneumonia and paralytic ileus. Postoperative complications occurred in 238 instances, with some cases having more than one disorder. Only 21.8 per cent of the patients studied had any morbidity and the total deaths in the entire series numbered 40. The most common causes of death were pneumonia, cardiac failure, pulmonary embolus, peritonitis and cerebral hemorrhage.

(This statistical study of a large series of hysterectomy cases is an interesting one. The mortality rate of 40 in the 1771 cases (about 2.27 per cent) is higher than is reported by some, and the proportion of injured ureter, torn bladder or torn bowel (1.6 per cent) may likewise seem a little high, but the series is obviously an unselected one, and no doubt included many difficult cases. The author of the paper has long been an advocate of total hysterectomy when possible rather than the supravaginal operation, and this is reflected in the fact that in 71 per cent of his cases the total procedure was carried out. This impresses me as a good healthy proportion. In any large series of cases, even in the hands of expert operators, it seems to me that in something like one quarter of them discretion will prove to be the better part of valor. My own preference is always for the total operation, but in nearly a quarter of the cases the undesirability of leaving the cervix seems to me a definitely lesser hazard to the patient than insistence upon its removal in the face of obvious local or general hazards. —Ed.)

VAGINAL HYSTERECTOMY

B. M. SUTHERLAND

Melbourne, Australia

M. J. Australia, 2: 411-412, October 2, 1948

The writer discussed the conditions in which vaginal hysterectomy is suitable. In considering whether or not to perform the operations, the following points are helpful: (1) there should be some relaxation of the vaginal outlet; (2) there should be no fixity of the uterus, no pelvic adhesions or matting of the uterus to adjacent viscera, and no pelvic disease; (3) the fundus should be of such a size that it can be delivered through the vesico-uterine space without undue force or manipulation.

Prior to operation, the patient should be thoroughly investigated and treated for any abnormalities disclosed. Two points in regard to the operation are stressed. First, the vagina is difficult to sterilize because of its mixed flora and moist conditions, and second, the pelvic planes opened are not highly resistant to pathogenic organisms. A comparison of the figures for mortality and morbidity in the 3 types of hysterectomy at the Women's Hospital, Melbourne, shows that vaginal and total hysterectomy had the highest morbidity rates and vaginal hysterectomy had the highest mortality rate. The author urges attention to the preparation of the patient and of the operative field. He feels that benefit might accrue from the use of penicillin, the sulfonamide drugs and the anti-coagulants.

(The conditions which the author sets forth for the selection of vaginal hysterectomy are somewhat like those observed by most American gynecologists, while with some the operation is done only in certain cases of prolapse. On the other hand, the author's prerequisites would be considered far too restricted in those clinics in which vaginal hysterectomy is the preferred operation for routine use. In such clinics the operation is frequently and easily done in nulliparous women, and often also for the removal by morcellation of even rather large myomatous uteri.—Ed.)

EXPERIENCE WITH THE WERTHEIM HYSTERECTOMY
IN OKLAHOMA CITY

J. W. KELSO

Oklahoma City, Oklahoma

South. M. J., 41: 906-909, October, 1948

This paper is a preliminary report of 25 cases subjected to the Wertheim hysterectomy as an adjunct to the treatment of carcinoma of the cervix. A summary of results is presented. There was no mortality or fistula and only one case of recurrence. Successful management of cases extensively operated upon calls

for careful preparation. Indwelling catheters facilitate the ease with which the operation can be done and aid materially in preventing urethral injuries. Preoperative preparation with penicillin was of unquestionable value. Skilled anesthetists, with the use of spinal anesthesia, aided materially in reducing the hazards of prolonged surgery. Adequate blood replacement during the operation to combat shock and adequate maintenance of fluid and electrolyte balance are considered essential. Postoperative use of liberal quantities of antibiotics unquestionably has allowed such extensive surgery to be done with a low mortality rate.

(See comment on abstract of paper by Read, below.—Ed.)

RADICAL PANHYSTERECTOMY (WERTHEIM) AND RADICAL PELVIC LYMPHADENECTOMY: A PRELIMINARY REPORT OF SEVENTY-FIVE OPERATIONS

W. L. THOMAS, B. CARTER AND R. T. PARKER

Duke University School of Medicine, Durham, North Carolina

South. M. J., 41: 895-902, October, 1948

The term Wertheim operation as used in this country should be understood to designate a radical panhysterectomy but should not be confused with the operation of radical hysterectomy with the added procedure of radical lymphadenectomy. The latter combined operation is a formidable procedure but can be performed with relative safety if due precautions are taken. The combined procedure has been employed by the authors in 75 cases with no mortality. The absence of deaths was attributed to the careful selection of patients, careful selection of anesthetic agent, blood transfusions, chemotherapy and antibiotics. Seventy-six per cent of the cases in this study who at operation showed metastasis are living and only 10 per cent of the entire series are now dead or living with cancer.

The authors feel that this is the procedure of choice in cancer of the cervix complicated by pregnancy. The combined operation is also of value in adenocarcinoma of the cervix. In patients who have received previous radiation the technical difficulties do not present a major problem; however, preoperative irradiation does seem to predispose to the formation of bladder fistula. It is concluded that the majority of patients with carcinoma of the cervix will continue to be treated with the accepted technics of irradiation therapy, but the problem of radical surgery demands further critical and careful analysis to determine its place in the treatment of cancer of the cervix.

(See comment on abstract of paper by Read, below.—Ed.)

THE ROLE OF SURGERY IN THE TREATMENT OF CARCINOMA OF THE CERVIX

C. O. READ

London, England

Am. J. Obst. & Gynec., 56: 1021-1036, December, 1948

The author has pointed out that in any discussion on the treatment of carcinoma of the cervix, division of opinion invariably centers around the relative merits of radiation and radical surgery. However, it is generally agreed that surgery is applicable only in Stages I and II. One of the most extensive studies of radical surgery, namely, the Wertheim operation, is that of Bonney. Most of his cases fell in Stages I, II and III. His operative mortality was 14 per cent and the 5-year cure rate was 58 per cent in those without gland involvement and 23 per cent in those with regional metastasis. With these results, the author has compared the results of radiation at the Marie Curie Hospital. The 5-year survival in these cases was 80 per cent for Stage I, 61.5 per cent for Stage II, 31.4 per cent for Stage III, and 7.2 per cent for Stage IV. The writer feels that, on the basis of these results, even the most biased surgical enthusiast must admit that overall and in general the results of radiotherapy are superior to those of surgery in respect to operative mortality and possible survival. However, with the newer refinements of surgery, the operative mortality can be substantially reduced and radical surgery continues to have a place in the treatment of carcinoma of the cervix. More careful selection of patients for surgery is certainly a most important consideration.

The indications for the Wertheim operation are limited but quite definite. Radioresistant tumors which fail to improve clinically after a period of radiation and which show resistance by biopsy examination should be treated surgically. Columnar cell carcinomas are usually quite radioresistant, and the results of the Wertheim operation are much superior to those of radiation in this type of tumor. The presence of large fibroids, ovarian tumors or salpingitis contraindicates radiation and such cases should be treated surgically if the patient's condition permits. Vaginal vault stenosis makes adequate radiation impossible. Pregnancy complicating cervical neoplasms is open to question but in the author's experience surgery has been the procedure of choice. It is also felt that the Wertheim operation is justifiable after a previous course of radiation therapy if the tumor is still in stages I and II.

The author points out that the figures given for radiation always tend to favor that form of therapy, as the 5-year results are described as "survivals" and not as "cures." However, a large percentage of 5-year survivals are literally dying of cancer of attenuated virulence and the 10-year survival rate shows a very appreciable drop, and even after this time a considerable percentage of patients die of the remote sequelae of radiation. Yet it remains true that the routine treatment of election for the average case of cancer of the cervix is by

radiotherapeutic means, but in certain cases there is a place for surgery. The author also suggests the more extensive practice of lymphadenectomy, especially in Stage III cases. This might be most applicable after a course of radiation therapy.

(The author of this paper, one of England's outstanding gynecological surgeons, was for many years associated with Victor Bonney, who for the long period during which irradiation was the almost universal method of treating cervical cancer, was perhaps the leading exponent of surgery in a limited group of cases. Read has become a distinguished successor of Bonney in his own country. Only a few short years ago those who did many radical operations for cervical cancer were looked upon as somewhat out of step with the army, but a reading of Read's paper impresses one with the fact that his attitude is far more conservative than that of a good many surgical enthusiasts in our American clinics.

Carter and his group are among those who have been doing the radical operation, with gland excision, in selected cases of cervical cancer. Their report of 75 cases with no mortality stresses perhaps the leading reason why radical operations have been revived, i.e., the fact that the primary mortality has been so tremendously lowered by such modern surgical advances as transfusion, antibiotics and chemotherapy. I would like to endorse the conservative last sentence in the abstract of the paper by Carter and Parker.—Ed.)

TOTAL VERSUS SUBTOTAL HYSTERECTOMY

S. E. CRAIG

Perth, Australia

M. J. Australia, 2: 407-408, October 2, 1948

The writer states that although total hysterectomy is the ideal at which to aim, at times circumstances render the subtotal operation advisable. Not every operator can perform the major operation without subjecting the patient to an operative risk far greater than of the development of carcinoma in a benign cervix. The most important deciding factor in the choice of the procedure is the capability, or otherwise, of the operator.

There is the problem of the lacerated, eroded and infected cervix; if it can be removed at the one session, the patient is better without that local septic focus. But in the author's experience such a cervix is not particularly liable to the development of carcinoma. Munnell (1947) recorded 215 total removals and 1533 subtotal removals. The respective mortality rates were 2.32 per cent and 1.76 per cent, a considerable difference. Munnell considered that most lacerated and infected cervixes did not develop cancer. The writer does not wish to discount the danger of carcinoma developing in the stump, but believes that the operator should impartially balance his own capabilities against the conditions found at operation.

(A short and succinct expression of a sensible attitude concerning this question. As to the incidence of cancer in the residual stump after subtotal hysterectomy, this is only one of

the considerations which, to my mind, make retention of the cervix undesirable. A persistence of cervical leucorrhea is frequent even after local treatment of the cervix, but even more worrisome is the not infrequent occurrence of bleeding as a result of intracervical granulation tissue, stricture of the os, and at times of persistence of slight and irregular menstrual bleeding, when small areas of residual endometrium are included in the stump. The benign nature of such bleeding, however, can never be assumed, and the patient is often obliged to submit, sometimes repeatedly, to cervical biopsy and curettage of the endocervix.—Ed.)

MYOMECTOMY

R. FOWLER

Melbourne, Australia

M. J. Australia, 2: 404-405, October 2, 1948

The surgeon's objective is an expeditious and complete removal of fibroid tumors with a view to preserving a competent uterus. The realistic surgeon will consider 4 alternatives: (1) watchful expectancy; (2) myomectomy; (3) radiation therapy; and (4) hysterectomy. When childbearing does not enter the picture, a difficult myomectomy is not justified in order to conserve a non-fertile uterus; hysterectomy is safer, affords a lasting cure for the fibroids and a refuge from future malignant disease. In pregnancy complicated by myomata, watchful expectancy is the rule, but in the early months myomectomy might be indicated. If the tumors make cesarean section necessary at term, the operation should be completed by hysterectomy. Myomectomy is mainly to be considered in the treatment of non-gravid "prospects." The decision between myomectomy and hysterectomy often will be made at the operating table, and the patient should be warned of this uncertainty.

(A short and pithy summary of a sound attitude in the management of myoma.—Ed.)

SURGICAL TREATMENT OF UTERINE MYOMATA

ARNALDO DE MORAES AND ALIPIO A. CAMELLO

Rio de Janeiro, Brazil

Obst. y Ginec. Latino-Amer. 6: 463, 1948

This paper deals with the therapeutic plan followed in cases of uterine myoma at the Department of Gynecology of the University of Rio de Janeiro, Brazil, where the senior author is Professor. It should first be emphasized that all cases of uterine myomata reported to that clinic are subjected to surgical treatment,

due to the fact that surgery may be more conservative than radiation. Furthermore, surgery eliminates the hazard of leaving behind any sort of potential malignancy. The authors' surgical plan of treatment is always preceded by uterine curettage, so as to detect any occasional malignancy of the endometrium besides permitting the systematic study of the uterine mucous membrane. In the younger group of women, surgery ought to be conservative (myomectomy) attending to reproductive function. If this cannot be accomplished, efforts should be made to conserve at least menstrual function, by performing fundectomy or partial hysterectomy and myometrectomy. In women beyond the age of 40, preference should be given to panhysterectomy, either by the abdominal or vaginal route, in view of the hazard of the development of cancer in the cervical stump. There are, of course, a few cases in which, for some reason or another, subtotal hysterectomy is the operation of choice. This surgical trend has been followed at their clinic since 1946 as the following figures will show. From September, 1936 to July, 1948, 293 patients were operated upon for uterine myomata, as follows: cervical amputation (cervical myoma) 1 case; myomectomy 35; myometrectomy 28; fundectomy and partial hysterectomy 38; subtotal hysterectomy 136; total abdominal hysterectomy 37 and total vaginal hysterectomy 17. One patient died during anesthesia. These figures can be divided into 2 periods: one from 1936 to 1945, and the other from 1945 to 1948. In 1945, conservative surgery was performed in 52.7 per cent of the cases; subtotal hysterectomy in 38.8 per cent and total hysterectomy in 8.3 per cent. In 1946, the percentages of the same operations were: 27.0 per cent, 43.2 per cent and 29.7 per cent. In 1947; 20.0 per cent, 20.0 per cent and 60.0 per cent. In 1948: 61.5 per cent, 7.6 per cent and 30.7 per cent. Hence, there was an increase in the number of total hysterectomies and, on the other hand, a decrease in the number of subtotal hysterectomies.

(The authors state that "all cases of uterine myoma are subjected to surgical treatment," but I feel sure that they refer only to those cases which call for some form of active treatment. They would probably agree that a small symptomless myoma in a woman of middle-life needs no treatment other than periodic examination. The menopause brings about regression in size, and the possibilities of malignant changes are numerically slight. In our own laboratory, the incidence of sarcomatous change in myoma was only 0.56 per cent (Novak and Anderson, *Am. J. Obst. & Gynec.* 34: 740, 1937). In some reports the incidence has been even less, while in others, such as that of Kimbrough (*Am. J. Obst. & Gynec.* 28: 723, 1934) it has been somewhat higher, Kimbrough's figure being 1.02 per cent.

In this country, as in the clinic of Rio de Janeiro, the surgical plan has apparently pushed into recession the radiotherapeutic management which at one time was carried to an extreme. Not many gynecologists now take too seriously the advice formerly publicized, chiefly by radiologists, that surgery should not be resorted to unless the tumor was larger than a 3 months pregnancy, or of submucous type, or complicated by pelvic inflammatory disease or producing pressure upon surrounding viscera. In the first place, it is not always possible to determine these characteristics preoperatively. I am sure that many surgeons, in selecting nice, movable fibroids when planning to put on a show, have been unpleasantly surprised that the apparently movable fibroid was complicated by extensive pelvic inflammatory disease and widespread intestinal adhesions, so that the exhibition of the surgeon's prowess was often much less glamorous than he would have wished. Nor are submucous myomas always easily diagnosed.

Again, the radiotherapeutic plan is limited to women approaching the menopausal age. At other age periods the woman can much more readily spare her uterus than her ovarian function. There are still other limitations of radiotherapy which might be discussed. All this does not mean that it has no place, because in the practice of most of us it does. In the comparatively small tumors in the premenopausal age, where the only symptom is abnormal bleeding, which incidentally is very often not due to the tumor but to a dysfunctional factor, the treatment can be like that of functional bleeding at this age period, diagnostic curettage followed by radium or X-ray abolition of ovarian function.

It is of interest to note that in the authors' clinic, as in most clinics in our own country, there is a strong trend toward total rather than subtotal hysterectomy, although perhaps not quite so pronounced as in many of American clinics. Interesting, too, is the considerable proportion of myomectomies in the series, indicating a healthy conservative policy in patients of the younger age group in whom the retention of procreativeness is usually such an important consideration, and one which is so often fully justified by the subsequent occurrence of pregnancy in previously sterile women. In our own country I believe there is an increasing popularity for myomectomy in properly selected cases, but unfortunately there are still a good many operators, especially among the general surgeons, to whom the mere presence of a myoma, large or small, with or without symptoms, seems to spell hysterectomy, regardless of the age of the patient and the possible importance to her of subsequent childbearing.—Ed.)

INTESTINAL OBSTRUCTION AND MYOMECTOMY DURING PREGNANCY

E. O. STRASSMANN

Houston, Texas

M. Rec. & Ann., 43, February, 1949

The case is reported of a 25-year-old white woman who was seen in her third month of pregnancy with acute abdominal pain. A diagnosis of intestinal obstruction was made and a laparotomy was performed. The obstruction was caused by adhesions between the posterior abdominal wall and a loop of the lower ileum. The uterus was the size of a 5-months' pregnancy and there was a large fibroid (13 cm. in diameter) occupying the lower two-thirds of the uterus. After careful deliberation, a myomectomy was performed and the uterus was closed as in a cesarean section. Postoperatively, the patient did well and the fetus continued to develop. In the 36th week of gestation a classical section was done and a living and normal male child was delivered. The mother and the child progressed normally.

The writer concludes that when faced with intestinal obstruction during pregnancy, operation should be performed as soon as possible. If the obstruction is caused or complicated by a degenerating fibroid, a myomectomy should be attempted in order to save the life of the baby and the fertility of the mother. The conservative approach to this problem has been made more rational by newer operative techniques and the antibiotics. 3 figures.

(An unrelieved intestinal obstruction, regardless of its cause, can be just as fatal in the pregnant as in the nonpregnant woman, so that, with proper qualification as to diagnostic and conservative preparatory measures, there will be no disagreement as to the necessity of operation in such cases, which fortunately are relatively rare. As to the myomectomy which was also performed in this patient, there is greater room for differences of opinion, as many women go through pregnancy quite normally with much larger tumors than the one described. On the other hand, myomectomies have often been excised without interrupting gestation. I recall a case in which a 12 pound tumor, fortunately of pedunculated subserous type, was thus excised at the third month because of the increasingly distressing pressure symptoms it had produced. Myomas not infrequently undergo degenerative changes in pregnancy, with resulting acute symptoms which can simulate acute appendicitis, acute cholecystitis or other such conditions. Operation, with myomectomy, is only rarely indicated, as the acute symptoms usually subside within a week or ten days.—Ed.)

WIDE CONIZATION OF CERVIX: FOLLOW-UP OF ONE THOUSAND CASES, SIX HUNDRED FROM TWO TO FOURTEEN YEARS

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Washington University School of Medicine, St. Louis, Mo.

Am. J. Obst. & Gynec., 57: 187-206, January, 1949

The author has reviewed the important historical steps which were made in the treatment of chronic cervicitis. In 1935, the author first reported the use of a cutting electrode for the wide conization of the cervix, and the present paper is a detailed analysis of a series of 1021 cases which were treated by this method. Of the total cases, 634 have been followed for periods of 2 to 14 years. In 727 of these cases, in addition to conization, anterior, posterior and lateral sutures were used to turn in the cervical mucosa.

Wide conization with suturing heals as well and gives as good ultimate results as the excellent Sturmdorf operation, and without the profuse bleeding and troublesome hemostatic measures which constitute a regular feature of the Sturmdorf procedure. Postoperative bleeding was not troublesome, owing to the hemostatic effect of the high tension cutting wire. In the few cases in which bleeding did occur it was stopped promptly with a single tamponade. Strictures occurred in only 16 of the cases and all but 3 of these cases were treated by office dilatation. Routine postoperative prophylactic dilatation to prevent strictures was not felt to be of any value.

As to the percentage of cures, there were only 14 of the total series who required reoperation and 67 who needed some additional minor treatment to effect a cure. This gives a cure rate of 91 per cent from the primary conization and a major portion of the remaining 9 per cent cured by some additional treatment.

The question is raised as to whether conization would influence subsequent pregnancies and labors. In this series there were 63 subsequent deliveries at or near term. Forty-nine of these were first deliveries following the conization, and

in none of these was there any evidence of trouble from the operation. The author feels that there is no substantial reason for denying the benefits of conization to women of the childbearing age.

In this series, in which the procedure was carried out for the sole purpose of treating chronic cervicitis, 16 patients were discovered to have early carcinoma of the cervix. Endometrial curettage is combined with the wide conization routinely. The specimens of the endometrium and removed cervical tissue can be examined microscopically when this operation is employed and because of the depth of the conization there is no distortion of the cervical histology. All of these cases of cancer, with the exception of one who refused further treatment, are alive today because of the early diagnosis of the lesion. In addition, wide conization for cervicitis definitely reduced the incidence of subsequent cervical carcinoma. None of the 1005 cervicitis patients developed cervical cancer during the period of observation. 8 figures.

(The results reported by the author in his large series are good, but the plan of treatment recommended by him would seem to be indicated in only a fraction of all cases of cervicitis, and even then the operator's individual preference for any one of several procedures would be likely to dictate the method. No rule of thumb can be applied to the treatment of chronic cervical inflammatory lesions. In a very large proportion, especially those with even large erosions, sometimes retention cysts, and often considerable hypertrophy, I believe that the common method of radial electrocauterization, if adequately and properly performed, gives excellent results. It is amazing to find how a cervix of the type described is transformed by such a procedure into one which, if examined some months later, looks essentially normal. It need scarcely be said that if there is the slightest clinical suspicion of cancer, cauterization or any other conservative cervical operation should be preceded by either the ordinary scalpel or punch biopsy or one of the various methods of surface biopsy.

But cauterization is both illogical and unsuccessful in the deeper lying intracervical infections, and the surgeon has to choose between conization, tracheloplasty of the Sturmdorf type and amputation of the cervix, the latter being of course restricted to patients beyond the childbearing age. I do not believe that conization, whether by the original Hyams technique or any modification of the latter, is completely free of the hazards of stricture and hemorrhage. It seems probable that these risks might be lessened by Crossen's method, which is a sort of combination of wide conization and the Sturmdorf method of mucosal covering of the stump. Personally I do not see any great advantage over the Sturmdorf tracheloplasty itself, nor do I think the latter should take any appreciably longer time. It is true that in the occasional case, where the vagina is small and the cervix high and perhaps fixed, it may be rather difficult, but in the vast majority this is not so. It does not interfere with subsequent pregnancy, and rarely is there any worthwhile bleeding, and I personally have seen no strictures.

Finally, in women beyond the menopause, a properly performed circular amputation of the cervix seems to me the best plan if there is extensive cervicitis, since it cures the latter and removes forever the hazard of cervical cancer.—Ed.)

SURGICAL TREATMENT OF RETRODEVIAION AND OF PROLAPSE
OF THE UTERUS

PERSONAL TECHNIC OF HYSTEROPEXIA

P. BARATA RIBEIRO

An. brasil. de ginec., 24: 3-24, October, 1948

The neo-ligamentous hysteropexia is restricted in its use to certain cases of retrodeviation and prolapse of the uterus, and it is especially indicated in prolapse of the uterine stump and vaginal vault. In retrodeviation it is the operation of choice when the round ligaments are atrophic or in cases of recurrence where the round ligaments have been previously used. Women who still want children or those subjected to violent abdominal effort such as is the case with asthmatics with uterine prolapse are benefited by the neo-ligamentous hysteropexia.

The author has described a new technique for the treatment of retrodisplacement and prolapse of the uterus. This technique essentially consists of freeing aponeurotic bands from the fascial sheath of the rectus abdominal muscles. These fascial bands are threaded through the internal inguinal ring and along the course of the round ligament. They are attached at the normal round ligament uterine junction or across the anterior surface of the uterus, depending on the degree of suspension required. All of this procedure is carried out transperitoneally, but the resulting suspension bands lie retroperitoneally and along the normal channels.

The author has reported 21 cases in which this operation was employed with very favorable results. Twenty of these cases showed complete correction of the underlying condition. Pregnancy can occur and progress normally and labor is unaffected by the neo-ligamentous hysteropexy. 19 figures.

(The author's term "neo-ligamentous hysteropexia," is obviously based on the fact that the operation which he describes makes use, not of the normal uterine ligaments, but of the artificial fascial ligaments which he fashions from the rectus fascia. I cannot believe that such a procedure would often be necessary, and, without ever having done it myself, I would think that it might often be awkward, and that there might be difficulty in estimating the lengths of the fascial strips and perhaps some risk of interfering with the blood supply. I am well aware that somewhat similar utilization of fascial strips has been made by various surgeons in abdominal suspension or fixation operations for the cure of extreme prolapse of the cervical stump or vaginal vault. However, I have always felt that the logical and the effective way for the cure of prolapse of an organ is to support it from below and not to hitch it up from above. That, however, has nothing to do with the operation described by Ribeiro as applied to correction of simple backward displacement. Failures after the proper employment of the usual suspension procedures, such as the Simpson modification of the Gilliam method, should not be common if cognizance is taken of the fact that such operations must often be combined with plication of the uterosacral ligaments. No matter how well an ordinary suspension is done, it is apt to be unsuccessful if the uterosacral ligaments are left markedly elongated, permitting the cervix to descend downward and forward in the axis of the vagina.—Ed.)

SURGICAL TREATMENT OF GENITAL PROLAPSE

F. VICTOR RODRIGUES

Brazil

An. Bras. Gin. 26: 365, 1948

The author reviews the different surgical procedures utilized in the treatment of uterine prolapse since the studies of Sorano, as well as the various types of operation devised to correct cystocele and vagino-perineal relaxation. The methods of fixation of the uterus and those utilizing the ligaments, since the works of Alquié (1840), are reviewed.

Modern procedures tend to rebuild the altered fascial structures, correct cervical elongation and rebuild the pelvic floor. Such aims can be obtained by the following technics: Mayo-Ward hysterectomy, interposition, Le Fort and Manchester operations.

The author reports a series of 82 cases of genital prolapse mostly treated by the Ward-Mayo vaginal hysterectomy or by the Manchester type of operation, with no deaths. In 76 cases local anesthesia was used. In all cases, immediate and late results were good.

STERILITY

RECENT ADVANCES IN THE TREATMENT OF INFERTILITY

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M. Rec. & Ann., 43: 718-720, January, 1949

As the basis for this study, 212 patients suffering from infertility were investigated and the causes of their infertility were listed according to frequency. Twenty-eight of the 212 patients became pregnant; several who were presumed to be pregnant did not return for examination and are not included in these successes.

The male was responsible either wholly or partially for the greatest number of infertile cases, 81, or 38.2 per cent. There have been few recent advances in treating unexplained cases of defective males. The author still relies on improving general hygiene, on the use of thyroid when indicated and on large doses of liquid vitamin B complex obtained from natural sources. This conservative therapy results in about 10 per cent becoming fertile. Recently, artificial insemination has been used, injecting half of a split ejaculate of the husband, since it was found that if the ejaculate is divided, the first half will contain about 85 per cent of the total spermatozoa. Under every circumstance, the necessity for doing a complete examination of the husband's semen cannot be overemphasized.

Next to male deficiency, the commonest cause of infertility in this series was a lowering of the basal metabolic rate to minus 10 or below. This occurred in 65 patients, or 30.6 per cent. Five of these patients became pregnant when the metabolism was raised but whether the thyroid was responsible for the pregnancy cannot be said.

Abnormalities of the cervical mucus were found in 34 cases, or 16 per cent, and the author feels that they would probably have been noted oftener if all the men working in the sterility clinic had considered it to be as important as he does. Mucus at ovulation is abundant, clean and thin and allows itself to be penetrated easily by spermatozoa. When specific vaginal and cervical infections are eliminated, the mucus may be abnormal because of: (1) a low grade non-specific endocervicitis; (2) endocrine imbalance; (3) cervical stenosis; or (4) tortuosity or acute angulation of the cervical canal. The author is convinced that the treatment of abnormal mucus should be conservative. Electrocoagulation and conization of the endocervix are still done too freely. Every time an electric current is put into the cervical canal or a cervix is coned there is a destruction of mucus secreting glands and the possibility of infertility is increased. Good results have been obtained from gentle dilatation of the cervix, massage of the canal with dry gauze and mild antiseptics. Sulfonamides given either orally or

locally in the form of cream will help, and recently success has been obtained in stubborn cases by giving 300,000 units of penicillin in bees wax a day for 3 consecutive days just after the period is over. A precoital douche of Ringers glucose solution will often improve the quality of the cervical mucus and in a definite number of cases will result in pregnancy.

From a mechanical point of view, it has been found that dilating a cervical stenosis, overcoming tortuosity of the canal, or eliminating sharp angulations will often make periods more regular as well as improve ovulation and the quality of the cervical mucus.

The question of ovulation, either lack of it or infrequency of it, is one in which great advances have been made, but at present this whole phase appears to be one of confusion. Hormonal studies are inconsistent as indicators of ovulation. Varied types of basal body temperature graphs make definite conclusions impossible. Biopsies taken at the right time always show ovulation except in those cases where the menstrual history shows that ovulation is not occurring. Vaginal smears seem to the author to be the most accurate tests, but the treatment of poor estrin phases or weak progestin responses is still most uncertain and unsatisfactory. The use of 1-2 gonadotrophic therapy of Hamblen has made some anovulatory patients ovulate, but never with consistent success.

The use of testosterone as an inhibitor of growth of endometriosis may allow some of these patients to become pregnant.

Tubal insufflations and hysterosalpingography continue to be the outstanding therapeutic measures in the treatment of infertility. At least 10 of the present patients became pregnant after one or the other of these procedures, although there was no absolute evidence that the tubes were occluded in any case.

Every effort should be made to win and keep the confidence of the patient by explaining fully everything that is done. If therapy takes us into the realm of the unproved, the patient should be so informed. The emotional factors involved in cases of infertility may actually be the ultimate cause of the infertility. Time, patience, understanding, and a certain facility in psychiatric methods are needed to treat this intangible difficulty.

(Among the interesting findings in this excellent study is that the male factor was the only factor or a contributing one in fully 38.2 per cent of the cases. Most of us will agree that the results of treatment of the male are in the main discouraging, and that the chief reliance must be put on general constitutional measures plus the use of thyroid. In sterility studies which are otherwise quite thorough, I have been impressed with the frequency with which basal metabolic studies of the husband are omitted, and yet they are certainly not less important than such studies of the wife, which are rarely overlooked. Certainly no one can be enthusiastic about the results in male patients of the various forms of gonadotrophic therapy which have often been resorted to.

The author makes a provocative statement when he calls attention to the fact that electrocoagulation and conization of the cervix are too frequently employed, and that they may be looked upon as two-edged swords, sometimes actually increasing the possibility of infertility. It is possible that this may be true, and that there may be justification for a return in some cases to the local antiseptic treatments of intracervical infections which have in recent years been frowned upon, without too quick resort to removal or destruction of the endocervix.

As for the anovulatory cases, everyone will share the author's pessimism as to methods of treatment, but not all will agree with him that vaginal smears constitute the best test for the occurrence or nonoccurrence of ovulation. On this point I still feel that, in spite of a few somewhat academic points which have been raised, the endometrial biopsy is as simple and accurate a method as we have available.

Finally, the author's emphasis on the value of psychological management of patients, and of explaining to them in simple language the whys and wherefores of the various steps of the investigation, cannot be too strongly endorsed.—Ed.)

NEWER APPROACHES TO FERTILITY STUDIES

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M. Clin. North America 32: 1533-1553, November, 1948

The author believes the customary insistence upon 2 years of unprotected coitus before considering a couple barren is an exaggerated standard. Primary sterility should be considered present after one year, and secondary sterility is present after 2 years when a woman has previously borne a child.

The essential factors controlling fertility are: production of a normal ovum, transportation of ovum to the prepared site of implantation, availability of normal spermatozoa to fertilize the ovum, insemination of the cervix and ascent of spermatozoa to the ovum. The physician must explain the multiple factors controlling fertility to the couple seeking help. He must emphasize the need for a complete diagnostic study and insist upon full cooperation from both husband and wife.

A minimal diagnostic survey is presented. To obtain an exacting medical history, a fertility questionnaire such as that of Weisman is suggested.

Male infertility is present in varying degrees in 50 per cent of the husbands studied. Physical examination should note any endocrine stigmata, abnormality of the genitals and adnexa, or alterations of the prostatic and seminal vesicular secretions. A complete appraisal of the semen as to volume, number of spermatozoa, percentage of normal and motile forms, should be made early in the survey. Testicular biopsy can be a valuable aid in selecting the treatment of azoospermia.

Gross pelvic abnormalities suspend further investigation until they are evaluated. The most frequent cause of infertility in women is either gonococcal or pyogenic inflammatory disease, resulting in tubal occlusion or chronic endocervicitis. Subclinical tuberculosis of the genital organs may be found.

Myomas of the uterus large enough to exert pressure on the neighboring organs, require myomectomy. Malformations of the uterus may be visible or palpable and can be studied by radiography. Large, grossly recognizable cystadenomas of an ovary require cystectomy.

Penetration of the cervical mucus by a large number of spermatozoa is essential

and necessitates a proper deposition of semen and a salutary state of the cervical canal. The Sims-Huhner test as a means of studying these factors is discussed and a basis for interpretation is briefly presented.

An evaluation of tubal function by means of the Rubin test or by uterosalpingography is indispensable. Contraindications to the procedures are acute or chronic pelvic disease, uterine bleeding or imminent menstrual flow, too recent intrauterine manipulation or history of temperature and pain following previous test. The technic and interpretation of the Rubin test is described. The use of uterosalpingography to locate the site of obstruction is discussed.

Dysfunctional menstrual disorders, amenorrhea and abnormal bleeding, permit the assumption that an endocrine fault exists. The diagnosis of regular anovulation must be established by repeated observation. The biphasic fluctuation of body temperature in association with the menstrual cycle is the most expedient method of observing ovarian function. The histology of the premenstrual endometrium obtained by biopsy or curettage provides information concerning ovulation, formation of corpus luteum and endometrial responsiveness.

(This is a very comprehensive resumé of the whole subject of infertility, and the ideas expressed are in conformity with those generally held. It has been my impression that most gynecologists advise sterility studies if pregnancy does not occur after one year rather than 2 years of married life without contraception. It is amazing, however, to note the patience and the undue delay shown by many couples in this respect, the gynecologist not infrequently being consulted only after many years of unproductive married life. The chances for successful treatment are sometimes definitely lessened by such delay. There are other couples who for economic or other reasons practice contraception for a good many years and then decide to have a baby. Not infrequently they find that the delay has caused them to miss the boat through the development of some such condition as endometriosis or myoma.—Ed.)

THE BIOLOGICAL ASPECT IN TREATMENT OF THE INFERTILE MARRIAGE

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Brit. M. J., 2: 851-853, November 13, 1948

Now that the role of the hormones of human gestation is becoming clearer, it is likely that the treatment of infertility will swing a little away from the mechanical aspect toward the medical and biological side. It has become the author's practice to initiate medical treatment aimed at securing implantation of the ovum in nearly every patient in whom there is no gross pathology. This treatment consists of instructing the patient to concentrate intercourse on the fertile dates, with abstinence from intercourse for a week or 10 days prior to

these fertile days, and to take from the first fertile day 0.6 mg. of dienestrol and 10 mg. of ethisterone daily. These hormones are continued until the onset of the next period or, if pregnancy occurs, until the eighteenth week of gestation. On such medical treatment alone, to the author's knowledge, 34.2 per cent of his patients have become pregnant, out of a total of 111 cases in which there had been no previous pregnancies. All but 3 of the 38 patients who conceived gave birth to live babies.

This method of treatment also has application in cases of repeated miscarriages and in cases of infertility due to inadequate semen. In 38 patients who had each had at least 2 miscarriages and none of whom had carried a baby to term, 28 became pregnant within 6 months and 20 carried their babies to term.

The writer believes that it is eugenically unsound to continue to boost a pregnancy by means of hormones after the eighteenth week, since by that time the function of the corpus luteum is over and the embryo should be able to elaborate its own hormones from then onward.

(I can see no particular objection to the plan of advice and endocrine therapy advanced by the author, but I hope that he does not mean, as may be gathered from the abstract, that he resorts to it in "nearly every patient in whom there is no gross pathology," without first ruling out such very frequent causes of infertility as tubal closure or impairment and seminal inadequacy.—Ed.)

THE ROLE OF SPECIAL DIETS IN THE TREATMENT OF FEMALE INFECUNDITY

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Brit. M. J., 2: 847-851, November 13, 1948

Refractory cervical block is a common cause of infecundity in overweight women between the ages of 30 and 40. The present paper concerns the investigation of 88 women in this age group with a history of primary or secondary sterility. These patients had severe impairment of cervical receptivity (complete absence of sperm invasion, or sparse and shallow invasion with rapid inactivation of sperms). In all cases pathogens or suspected pathogens were recovered from the cervical mucus, with the exception of Neisserian infection. All patients showed distinct overweight, i.e., more than 10 per cent above the mean weight for age and height. This series of cases was characterized by the absence of response, or partial response only, to treatment with antibiotics and estrone.

The authors found that the refractory cervical block tended to respond to treatment with antibiotics and estrone if loss of weight were first procured by dietary measures. Because of the predominance of infections by organisms of intestinal type, the dietary regime was in the direction of an attempt to reorganize

the intestinal flora. The main characteristic of the diets was the exclusion of sucrose, with concomitant increase in other foods chosen to produce a diet adequate for maintenance and reproduction within the limitations imposed by rationing. One group of patients was put on a sucrose-free diet with administration of lactose, a second group was given a sucrose-free diet without lactose, and a third group was given a supplemented sucrose-free diet which, in most cases, involved an increase in caloric intake. The results in regard to cervical response and weight changes are shown in Table II.

TABLE II

DIETARY GROUP	NO. OF CASES	CASES SHOWING LOSS OF WEIGHT		CASES SHOWING NO LOSS OF WEIGHT	
		With Cervical Response	Without Cervical Response	With Cervical Response	Without Cervical Response
I. Lactose group (sucrose-free).....	14	9	2	—	3
II. Sucrose-free group (without lactose)...	65	45	12	2	6
III. Supplemented sucrose-free group.....	9	6	—	—	3

(While the importance of the cervix and a hostile cervical block as a possible factor in female infecundity has long been recognized and accepted, the authors' suggestion that this refractory block may respond to treatment with antibiotics, estrogen and a sucrose-free diet represents a rather new approach. The standing of the authors merits consideration of their suggestion, although the series of cases studied has very little statistical value, and one has the feeling that further studies will not yield any very important addition to our armamentarium in the management of infertility.—Ed)

PENETRATION OF CERVICAL MUCUS BY SPERMATOZOA: A METHOD OF INVESTIGATION

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Lancet, 2: 723-724, November 6, 1948

Previous methods for investigating the entry of spermatozoa into cervical mucus place both mucus and spermatozoa under considerable stress. The surface tension in mucus held between a slide and cover-slip, or in a capillary tube, must be very large relative to the energy of a spermatozoon. Dead spermatozoa may be drawn across the mucus film between slide and coverslip by capillarity, and there is a suggestion that suction acts in the capillary tube method, in that grossly abnormal forms have been found invading cervical mucus by this method. The authors describe a method for studying entry of spermatozoa into cervical mucus which was devised to reduce interference from surface tension. The special slide used is not unlike a Thoma counting slide with the grooves running parallel

to the long axis instead of transversely, but the strip between the grooves is at the same level as the rest of the surface. The central region is marked for 3 cm. with transverse etched lines 2 mm. apart.

The mucus is spread over the region of etched lines on the slide. About 0.05 ml. of semen is placed near one end of the mucus, and the drop is stroked with a platinum loop until the mucus is in contact with the semen for the whole width between the grooves. These grooves prevent the seepage of semen around the edges of the mucus and maintain a standard width of surface between mucus and semen. The slide is incubated at 37 degrees C and is examined under a $\frac{2}{3}$ in. objective at convenient intervals between 30 minutes and 3 hours from the beginning of the test. No coverslip is used. At examination, the slide is placed so that the line of junction between mucus and semen is in focus, and the slide is moved for each 2 mm. section until no spermatozoa are seen in 5 microscopic fields in each of 2 adjacent sections.

With this special slide different types of penetration can be compared by noting (1) the greatest distance reached by the spermatozoa in a given time, (2) their motility in the mucus, (3) the relative numbers of spermatozoa reaching points at various distances from the semen-mucus junction, and (4) the course of the spermatozoa within the mucus.

(The increased volume of the cervical secretion at the ovulation phase, but the decrease in its resistance to the penetration by spermatozoa has now been well established. It is only one of many examples of the remarkable timing and the teleological character of all the phenomena concerned in the reproductive cycle, the central actor of which is the egg, including especially its extrusion from the ovary and its safe delivery to keep its tryst with the gay spermatozoal intruder. The path of the latter to the rendezvous is normally made easier by the unlatching of the cervical door, but cervical pathology may interfere with this physiological unlatching. Just how frequently this is a factor in infertility one can not be sure, but it is one which must at least be reckoned with, and which appears to justify the increasing number of studies which are being directed to this point. The method described by the authors appears to be somewhat more precise and scientific than some of those which have been previously described.—Ed.)

SIMS TEST AND MALE INFERTILITY

GERTRUDE DEARNLEY AND MARY BARTON

London, England

Lancet, 2: 543, October 2, 1948

Miss Dearnley reviewed the development of the subfertility clinic at the Royal Free Hospital, London.

Dr. Barton chooses to do the Sims test in the late follicular or ovulatory stage. It should be supplemented by semen analysis, since it may mask pyospermia and does not reveal exfoliative conditions of the testis. When spermatozoa are found

in the fornix in reasonable quantities, but none in the cervical mucus, the husband's semen should be tested against the cervical mucus of another woman, and the wife's mucus against the sperms of another man.

(The abstract does not make it sufficiently plain that the testing of the husband's semen against the cervical mucus of another woman, and the wife's mucus against the sperms of another man, are purely laboratory procedures, involving no physiological cooperation between these various mates.—Ed.)

TUBAL INSEMINATION IN THE TREATMENT OF CERTAIN TYPES OF STERILITY

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An. Bras. de Gin. 26: 173, 1948

A historical review of artificial insemination is first brought up. As to the heterologous type of artificial insemination, one should consider the chances one is taking in performing it, whereas with the homologous type, the moral, religious, psychological, medical, legal and social problems are of no great concern. The author utilized both Dickinson's (tubal insemination) and Leventhal and Solomon's procedures in a few cases of sterility, which were divided into the following groups: 1) Couples with no apparent cause for the sterility complained of, which were submitted to Leventhal and Solomon's test. Two or 3 insufflations were performed within an hour or 3 hours following normal intercourse, between the 12th and 17th days of the menstrual cycle. In a total of 8 cases, pregnancy occurred in 4. Two other cases could not be considered as positive results, because pregnancy developed only after treatment had already been suspended for 4 and 6 months previously. 2) Couples in which sterility seemed to be caused by cervical hostility, presenting a negative Huhner test in spite of the fact that the cervicitis had already been cured. Homologous artificial insemination was practiced in this group, comprising 5 cases. One cubic centimeter of sperm obtained no longer than an hour following ejaculation, was introduced within the cannula insufflated into the uterine cavity. This was repeated twice or thrice monthly. Pregnancy occurred in 3 cases. 3) Couples in which oligospermia and relative oligospermia appeared as the only cause of sterility. The same technic described in group 2 was used in this group of 3 cases. Pregnancy developed in 2 cases.

All these cases concerned primary types of sterility varying from 2 to 5 years in duration. The couples' ages varied from 24 to 33 years for the women, and from 24 to 36 for the men. No secondary effects were noticed. Contraindications for insufflation were strictly observed, and the use of small amounts of sperm constituted the rule in every case.

(This idea of propelling lazy spermatozoa up into the genital canal by gas pressure seems like a rather random affair. If a spermatozoon does not have vitality and motility enough to migrate to the tube, it would seem doubtful that it would be capable of fertilizing the egg, even if the latter has not been blown out of the tube by the gas pressure. The enthusiasts for artificial insemination appear to be becoming more conservative about injecting semen even into the uterus, much less the tubes, for fear of infection, and many now place the semen in the vaginal fornix. There are still other theoretical objections to this idea of tubal insemination, and I doubt whether it will appeal to many gynecologists.—Ed.)

UTEROTUBAL INSUFFLATIONS

A. SHARMAN

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Lancet, 2: 542-543, October 2, 1948

Tubal spasm is a common cause of negative findings in the Rubin insufflation test, and the author has found that only 32 per cent of cases showing non-patency on a single test have occluded tubes. It is felt that the addition of a kymograph to the insufflation apparatus makes it possible to distinguish between normally patent tubes and those which are the site of spasm, stenosis or adhesions.

Dr. Jackson said that central abdominal pain associated with a tracing of the occlusion type generally means spasm, while pain, often milder, in the iliac fossa or at the back means occlusion. Gentle handling of the cervix is stressed.

HYSTEROSALPINGOGRAPHY

JOSEPHINE BARNES

London, England

Lancet, 2: 543, October 2, 1948

The author described hysterosalpingography with water-soluble radio-opaque media. She employs a watery solution of diodone. A viscous solution causes severe pain, but a watery solution does not cause spasm. An instantaneous radiogram is taken when the fluid is injected, showing the fluid taken up rapidly into the tubes and demonstrating any blockage. Twenty minutes later a radiogram is taken of the whole abdomen, showing excretion of dye already beginning in the kidneys. The whole procedure is complete in about one-half hour.

Dr. E. Friedman (London) said that he had used "Viscyszol" in nearly 50 cases without ill effects or complaint from patients. This preparation is 50 per cent diodone.

MISCELLANEOUS

VASCULAR CONGESTION AND HYPEREMIA: THEIR EFFECT ON STRUCTURE AND FUNCTION IN THE FEMALE REPRODUCTIVE SYSTEM

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Am. J. Obst. & Gynec., 57: 211-230, February, 1949

There still exists in gynecology a group of conditions of uncertain cause. These have the common characteristics of producing chronic pain without evidence of inflammation or other obvious pathologic process and include chronic mastitis, oöphoritis or cystic ovary, hypersecreting cervix and diffuse hypertrophy of the uterus.

For many years prior to about 1915 they were regarded as inflammatory. More recently they have been regarded as hormonal. The author feels that new factors are to be found in disturbances of the autonomic nervous system and associated abnormal vascular conditions.

The consideration of physiologic principles, the review of the literature and the analysis of the clinical material leads to 4 theses: 1. The circulatory mechanisms of the reproductive system are very labile and capable of rapid, extreme responses in local intravascular blood volume, as well as local extravascular fluid content, to hormonal, nervous and other factors. 2. These vascular changes in the vascular conditions are capable of producing pain, menstrual variations and secretory disorders. 3. These changes may be generalized throughout the reproductive tract. 4. The effects of congestion, hyperemia and edema are temporary at first, but if persistent, may result in permanent changes, chiefly hyperplasia of the connective tissue of the reproductive organs.

A typical case illustrating the general picture of the so-called "Congestive-Fibrosis" syndrome is reviewed. Here the characteristic symptoms and observable pathological results of a vascular and autonomic nervous system disorder is seen.

Four separate factors, acting alone or in combinations, may affect the pelvic circulation. The pelvic veins are usually dilatable, deficient in valves with weak attachments to the surrounding connective tissue support. Mechanical factors such as gravity and posture play a part in determining conditions in the pelvic circulation. Retroversion or prolapse may be associated with stasis or congestion.

Inflammation plays a role in the production of temporary hyperemia. There may be permanent effects in the form of parametritis.

The effect of estrogen is mainly arterial, resulting in a hyperemia. The storage of salts and fluids in the interstitial spaces is another result of estrogen.

The circulation of the pelvic organs is controlled largely by the autonomic

nervous system. Vasodilation may be produced by 3 types of stimuli: local sensory stimuli received in the external genitals; psychic stimuli of a specific sexual character and psychic stimuli of a nonsexual nature, such as worry, fear and tension. Patients having symptoms of genital tract congestion commonly suffer from emotional instability, radiating neuralgic pains, palpitations and indigestion also, indicating a strong autonomic factor in this syndrome.

A review of the literature leads to a more complete description of what may be called the Congestive-Fibrosis. The fundamental processes concerned are outlined in table 2.

TABLE 2
The Congestion-fibrosis Syndrome

	CONGESTION STAGE	FIBROSIS STAGE
Uterus	Uterine congestion	Diffuse hypertrophy
Cervix	Hypersecretion Endocervicitis and erosion	Hypertrophy
Parametrium	General pelvic congestion	"Chronic posterior parametritis"
Peritoneum	Edema Increased ascitic fluid	"Douglasitis"
Ovary	Congestion	Fibrocytic ovary
Breast	Premenstrual engorgement Mastodynia	Chronic (fibrosis) mastitis

This approach to the problem combines a very old gynecologic theory with the more recent field of psychosomatics. 5 figures.

(This is a difficult paper to comment upon, because it covers such a wide field of both lesions and symptoms, and because some of the author's concepts are of necessity hypothetical. He showed great courage in tackling such a diffuse problem, and in reviewing such an enormous literature. A good many of his references are to very old publications of the preceding century, and a good deal of his effort is directed toward a fitting of old concepts to more modern advances in pathology, physiology, endocrinology and even psychosomatics. The paper is extremely long, and some will no doubt consider it somewhat discursive and diffuse. That prolonged hyperemia tends toward fibrosis, which is perhaps the author's chief thesis, will probably excite very little disagreement, but my own reaction is that he tried to cover too much territory, and that this extension involves explanations of mechanisms which must be considered hypothetical. Coming as it does from a man of Taylor's standing, experience and ability, the article is a very provocative one, which well merits the time and concentration required for its evaluation.—Ed.)

CARCINOGENIC AND ANTICARCINOGENIC SUBSTANCES

E. C. DODDS

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Lancet, 2: 837-841, November 27, 1948

The writer discusses the various external and internal carcinogenic and anti-carcinogenic substances. A very significant fact which emerges from this study is that there are a great many ways of producing cancer, with no fundamental connection between them, but that, having once started the process, we have no means of stopping or checking it by direct action. All the anticarcinogenic substances and agents act indirectly.

The possible carcinogenic effect of the female sex hormone has been studied. There is now evidence that, if the strain of mice used as experimental animals is one in which spontaneous mammary tumors do not occur, the administration of estrone is without effect. However, in a strain with a definite incidence of mammary tumors, estrogen treatment causes a significant increase in that incidence. The same results are obtained with the synthetic estrogens, which indicate that the causal factor is estrogenic action, apart from molecular configuration. Important as these results are from a theoretical point of view, they do not constitute a contraindication to the clinical use of estrogens, since the doses given to human beings are fractional compared with those administered experimentally to mice. 14 figures.

(The author of this paper has for many years been a leader in the study of problems dealing with experimental carcinogenesis. Incidentally, it was Dodds and his group of collaborators who, as an important by-product of their work in this field, discovered the remarkable estrogenic properties of certain non-hormonal chemicals, especially the stilbene group, the chief representative being the now widely employed diethylstilbestrol. In spite of the widely prevalent abuses of the latter, its introduction marked a milestone not only in the studies of estrogens, but also in the field of therapeutics, chiefly because of the cheapness of the substance as compared with the natural hormones, and its great potency when administered orally.

The conclusions expressed by Dodds in the present paper are in conformity with those reached by American investigators, especially Gardner and his associates, who have studied similar problems so assiduously and so profitably. Even when estrogens incite cancer in the experimental animal, these authors have emphasized that the fundamental role of the genotypic factor can not be excluded. After all, this appears to be the simple crystallization of the immense amount of cancer research in all fields of science, as I tried to simplify it in a recent paper of my own (J.A.M.A. 135: 199, 1947). Two factors appear to be concerned in the production of cancer. One of these is some still unknown predisposition residing in the genes, and in this we must include the possible role of heredity, though not necessarily in the sense implied in Maude Slye's work. In some individuals this genotypic predisposition is so strong that the irreversible change which converts a normal body cell into the killer cell of cancer, whether we give this the name of somatic mutation or apply some other designation, is bound to occur, and cancer of some organ or tissue is inevitable. On the other hand, much evidence has accumulated to indicate that the intrinsic cell changes are subject to influence by such extrinsic factors as trauma and irritation, whether the latter be in-

flammatory, chemical or endocrine in nature. After all, the endocrines are chemical substances, and their prolonged administration might be expected to incite cancer just as do the hydrocarbons which have been found to be so carcinogenic in animal experimentation. It would thus appear that in many cases the development of cancer is contingent upon the genotypic factor plus some extrinsic irritation, possibly endocrine in nature. Finally, there are the happy individuals in whom the genotypic factor is so diluted that cancer does not develop regardless of the degree and duration of inflammatory and endocrine irritation.

Homely and oversimplified as the above grouping is, I believe it to be in keeping with the present status of cancer research. This view fully justifies the wisdom of removing sources of chronic irritation, a practice which has been followed by gynecologists for many years, especially in the field of cervical pathology. It also justifies the frequent warnings against the indiscriminate and excessive therapeutic employment of estrogens.

On the other hand, it is refreshing that Dodds, who has been so long and so intimately linked up with the correlative study of estrogenesis and carcinogenesis, sees no contraindication to the clinical use of estrogens, chiefly because the doses involved are so minute as compared with those necessary to produce experimental cancer in laboratory animals. All this being true, I believe that he would probably agree, though this consideration is not included in the abstract, that no sensible clinician would wish to gamble with the prolonged administration of estrogens in menopausal women who, because of a presumably strong hereditary predisposition, or the presence of a so-called precancerous lesion, or with the history of a recently removed cancer, may be considered vulnerable on this point. Even in these I personally do not believe that modest and intermittent estrogen dosage carries with it any worthwhile risk, though one is often inclined in such cases to prefer testosterone, which gives somewhat less striking relief from menopausal vasomotor symptoms but is definitely less carcinogenic.—Ed.)

ADVANCES IN OBSTETRICS AND GYNAECOLOGY

J. WYATT

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Practitioner, 161: 256-260, October, 1948

The two recent outstanding discoveries with application to obstetrics and gynecology are the Rh factor and penicillin. It seems essential that the Rh factor of every pregnant woman should be ascertained: if it is found to be negative the husband should be investigated, and unless he is of a similar type the confinement should take place in a hospital where special treatment for both mother and baby is available if required. Penicillin is of value in gross puerperal infections and in cases of acute mastitis in the lactating breast. Prophylactically, penicillin powder, alone or combined with a sulfonamide, has been used with apparent success in cases where cesarean section must be carried out after the patient has been in labor some long time, or when vaginal interference has taken place. In gynecology, penicillin has not had much application, except in acute salpingitis which commonly follows either an infected abortion or gonorrhea. Provided suppuration has not occurred, penicillin may abort the attack, in some cases even leaving the tube patent.

In cases of stress incontinence in which simple local operation fails to bring relief, another technic is worthy of trial. Some years ago, use was made of the fascia covering the abdominal muscles, strips of this fascia being brought down behind the symphysis pubis and fastened around the urethral neck. The principle of this method is that when the patient coughs or strains the abdominal muscles are active; this automatically tightens the fascia and the urethra is thereby closed and urine prevented from escaping. A modification of this operation has been used with success in the author's country in recent times.

TERTIARY SYPHILIS OF THE UTERINE BODY AND UTERINE ADNEXA

W. DE SOUZA RUDGE AND D. DELASCIO

Obst. y Ginec. Latino-Amer. 6: 393, 1948

Although syphilis of the external genitalia, vagina and cervix uteri constitutes a well known and well established condition, syphilis of the body of the uterus, tubes and ovaries, on the other hand, is still a controversial pathologic entity.

Reviewing the whole medical literature, the authors were able to find only 3 definitely established cases of tertiary syphilis of the corpus uteri: 1 of Hoffmann (1911), 1 of Gellhorn (1918) and 1 of Billig (1928). A few others have been reported too, but with no definite pathological proof.

The case reported by the authors, the 4th of tertiary syphilis of the uterine body and the 5th of an identical lesion of the ovary in the whole literature, refers to a 23-year-old married female whose only complaint was hypogastric pain lasting for 3 months. Menstrual history was negative. Marital history revealed one delivery 8 years previously, and no miscarriages. Pelvic examination disclosed a tumor in the hypogastric region, presenting the size of a full-term fetal head, hard, and irregular in shape. Patient was operated upon under the impression of uterine myoma. After releasing dense and numerous intestinal and omental adhesions, subtotal hysterectomy along with bilateral salpingectomy and left oophorectomy was performed. The gross appearance of the uterine tumor measuring 12 x 8 x 5.5 cm. suggested myoma with malignant changes. Patient was discharged in good condition on the 8th post-operative day. Pathological report: tertiary genital syphilis, multiple gummatous lesions of the myometrium and ovary, and chronic salpingitis. In view of the latter report, a Wassermann blood test was performed, and the result was highly positive.

(Syphilis of the uterine body is so exceedingly rare that it should not be considered cautious to question every case unless the evidence is incontestable. So far as I know, there has never been a report of a primary lesion in the endometrium, in spite of the fact that the spirochete is mobile and that the endometrium is a tissue which is quite vulnerable to other forms of infection. As regards secondary syphilis, there is an almost equal dearth of

authentic reports, although I believe there are a few reports of the finding of spirochetes in the uterus in the secondary stage of syphilis.

When one considers the wide prevalence of syphilis, and the great frequency of tertiary lesions in many other organs, it is amazing how little knowledge we have on possible syphilitic lesions of the uterine body, especially since careful routine microscopic examination is the rule in all the laboratories of today. Through our own laboratory at Johns Hopkins Hospital has passed pathologic material from thousands of syphilitic patients, and yet I do not recall any case in which a diagnosis of syphilis of the uterine body was made. It is of course possible that certain cases of chronic endometritis and chronic metritis were produced by syphilis, but it has not been possible to separate these from other chronic inflammatory lesions through the finding of such features as perivascular infiltration, giant cells or gumma formation.

Probably the most assiduous modern investigator of the question of syphilis in relation to the female genital apparatus was the late George Gellhorn, and his various publications on the subject are still indispensable sources of information to those interested in this field. Among others, I would recommend his chapter on "Syphilis in Women" in volume 2 of the Curtis Obstetrics and Gynecology. Even though published in 1933, the chapter is far from obsolete, as comparatively little additional knowledge has accumulated since then.

The pathological report in the case reported by the authors, including the finding of "gummatous" lesions in the myometrium and ovary, would seem to justify the impression of tertiary syphilis. Spirochetes are notoriously difficult to demonstrate in tertiary lesions, and I do not know whether any effort was made along this line, nor is the microscopic evidence for the diagnosis available for comment. Anyone interested in this particular problem would probably wish to communicate with the authors for further details of this particular case.—Ed.)

THE VALUE OF THE PERIODIC EXAMINATION OF SUPPOSEDLY WELL WOMEN

CATHERINE MACFARLANE

Woman's Medical College of Pennsylvania, Philadelphia, Pa.

M. Clin. North America, 32: 1557-1561, November, 1948

An attempt is made to determine the value of the periodic pelvic examination in the detection of cancer of the uterus in the presymptomatic stage. A report is made on 732 women examined regularly for a period of 10 years.

Other abnormalities as well as cancer were detected and tabulated. The most important of the benign lesions from the standpoint of cancer are the 489 inflammatory lesions of the cervix, 214 of which were eliminated.

Only 8 pelvic cancers developed and 4 of these were detected on the first examination. The author attributes the low incidence of cancer of the cervix to the early discovery and elimination of inflammatory lesions.

The recommendation is made that every woman over 30 who has borne a child should be examined twice a year, single women over 30, once a year, and that inflammatory lesions of the cervix should be eliminated.

(The author of this paper, for many years the Professor of Gynecology in the Woman's Medical School of Pennsylvania, has been a pioneer in the detection of cancer in early and preclinical phases, and her 10 year study in Philadelphia was a valuable contribution. It is of interest that only 8 cases of pelvic cancer developed during the period of study of this large group, and since 4 of these were detected at the first examination, it may perhaps be assumed that only 4 were of the subclinical group. This may seem like a very small yield for such a long and painstaking study, but it must be remembered that the unearthing of very early cases is only one of the benefits of such undertakings. The prophylactic aspects of correcting or removal of chronic irritative lesions which may at least predispose to cancer must also be considered. Finally, it is safe to say that every patient included in this study will forever afterward be on the alert for danger signals and will probably continue to seek periodic examinations herself and inspire many of her friends to do likewise. Every cancer clinic, and for that matter, every doctor's office, should be a focus for the dissemination of education and advice along this line, and this can constitute no mean contribution to the anti-cancer campaign.—Ed.)

PSYCHOSOMATIC APPROACH TO GYNECOLOGIC PROBLEMS

R. A. MATHEWS AND W. R. O'BRIEN

Pennsylvania Hospital, Philadelphia, Pa.

M. Clin. North America 32: 1583-1599, November, 1948

That psychic factors play a prominent role in dysfunction of the physiology of the pelvic organs is understandable when we consider the many restraints our culture imposes upon the free expression of the individual's natural development. The influence of wishes and strivings, the strength of which is not recognized consciously by the patient, plays a role in influencing daily activities and the development of a complaint problem.

Biologically and psychologically the girl begins to function as a woman at puberty. She may rebel against the female role by suffering pain at each period. Or the girl's first period may be accompanied by feelings of guilt or fear of having been injured. The preparation for the menarche is too often hardly more than that dependent upon old folk lore. Correct information should be presented by someone with whom the child has a healthy emotional relationship.

The menstrual cycle is often interrupted or altered by emotional factors. The case of a young girl who did not menstruate for a year following a long conflict with her mother over social mores which culminated in a bitter hysterical scene is cited. Psychotherapy directed toward the relief of her guilt and the acceptance of her sexuality soon reestablished the menses.

An evaluation of dysmenorrhea must embody a consideration of the woman's entire attitude toward womanhood. The girl who looks upon menstruation as a part of growing up and of eventually having children, is not usually troubled with painful periods. A woman who is childless may find the period a depressing time. The woman who rejects childbearing may exhibit premenstrual tension and feel relief at the onset of the flow. Dysmenorrhea sometimes appears to be

of sufficient severity to justify active treatment, but consideration must be given to the patient's reaction to the reality of being barren. Frigidity in a woman involves a consideration of the meaning of the sex act to her. Woman's new position in competition with man conflicts with her unconscious need to remain passive. Fear of pregnancy, frank hostility towards the marital partner, psychically traumatizing events, and conflicts in other personality areas may cause frigidity.

Increasing evidence is accumulating to support the theory that emotional factors can cause apparent sterility. Recurrent or intractable nausea may represent a rejection of pregnancy.

It is the psychological response to the menopause which offers the woman her most difficult problem and results in a variety of symptoms. The woman with strong neurotic characteristics is more likely to develop involuntional melancholia or involuntional paranoia.

The authors present a short discussion of the principles of psychotherapy. The understanding of the mechanisms which are at work in the patient personality is of extreme importance. Therapy depends on the emotional relationship between the therapist and the patient, fostering growth in the direction of maturity. It is useless to moralize and it may increase the patient's conflict. The therapist should function as a catalyst in aiding the patient to form her own decisions and should not offer his personalized advice except in matters of specific medical treatment.

(Although I believe the authors are psychiatrists, they present a much clearer and more easily understandable discussion of the psychosomatic angles of gynecologic disorders than is usually found in the writings of psychiatrists, who seem so often to find it difficult to come down to earth and talk about such things except in a rather ethereal way and with a highly technical vocabulary which is likely to be unintelligible to the average reader. Every gynecologist knows how important a part is played by the patient's psyche in many gynecological disorders. Volumes could be written upon the various subdivisions discussed by the authors. As they say, it is especially important to envisage the psychosomatic factors in the management of the menopause. As a matter of fact, they are usually far more important than mere endocrine therapy, which is indicated in only a small fraction of cases.—Ed.)

THE HEPATO-OVARIAN SYNDROME

J. A. HUET

Acta Endoc. Gynaec. Hisp.-Lus. 1: 171, 1948

Under the designation of hepato-ovarian syndrome, the author includes a number of correlated and reversible disturbances of the liver and female genitalia resulting from hormonal imbalance, which gives rise to alterations on those organic systems. Pathogenetically, one should stress the great importance of the hepatic function in the metabolism of the female genital hormones and its anti-estrogenic activity. In the hepato-ovarian syndrome, hyper-estrogenism is responsible for the hepatic disturbances observed. If the level of absorption of the

liver is overpassed, excessive estrogenic hormone causes congestion and intoxication of the liver, which, in turn, reacts with signs of intolerance. On the other hand, hepatic deficiency, by impairing the normal excretion of estradiol, may originate disturbances of the hyper-hormonal type, especially an imperfect secretory transformation of the endometrium. Consequently, menstrual disorders and sterility can thus be explained in women suffering from liver diseases.

Based upon these correlative disturbances, the author devises a few therapeutic measures.

(This idea of a hepato-ovarian syndrome seems like a plausible one, and has been much publicized in recent years, especially through the work of the Biskinds. However, it is far from clearly established, and discordant voices are being raised against it. For example, a very able endocrinologist, Zondek, in a recent paper in collaboration with Brzezinski (J. Obst. & Gynec. Brit. Emp. 55: 273, 1948; see abstract and comment in Survey 4: 240, April, 1949) has recently published studies indicating that in both the pregnant and the nonpregnant woman vitamin B deficiency has not the slightest effect upon the estrogen-destroying capacity of the liver. And yet this idea has been already grabbed up by the therapists, and vitamin B therapy has been exploited by certain manufacturing firms as of great importance in the treatment of such disorders as functional bleeding. The basis for this whole concept is still a very shaky one.—Ed.)

HEPATOGENIC METRORRHAGIA OF PUBERTY

JOSÉ MEDINA

São Paulo, Brazil

An. Cl. Ginec. Fac. Med. Univ. São Paulo, 2: 11, 1948

The author studies the cases of metrorrhagia affecting girls during puberty, in which pelvic examination is entirely negative except for hypoplasia of the uterus. These forms of bleeding are apt to be more profuse when the uterus is smaller, approaching the so-called infantile type. The first explanation offered for these cases pointed to a deficiency of estrogen as the cause of the bleeding, in view of the coexisting uterine hypoplasia. However, estrogen therapy failed to cure such patients even though it was used in order to obtain growth of the uterus within its normal limits. On the other hand, hypoplasia cannot be taken as the cause of the bleeding since we do see patients with a small uterus menstruating quite normally, and, besides, in some instances bleeding takes place after the patient has had several normal periods since menarche. Unresponsiveness of the uterus to the growth-promoting effect of estrogen can explain uterine hypoplasia in those cases in which the other segments of the genital canal are normally developed. It does not, however, explain the cause of metrorrhagia. Blood dyscrasias should be searched for, but one occasionally sees cases with entirely normal blood tests. The finding of thrombocytopenia alone does not justify the diagnosis of the purpura hemorrhagica of Werlhof, in which,

of sufficient severity to justify active treatment, but consideration must be given to the patient's reaction to the reality of being barren. Frigidity in a woman involves a consideration of the meaning of the sex act to her. Woman's new position in competition with man conflicts with her unconscious need to remain passive. Fear of pregnancy, frank hostility towards the marital partner, psychically traumatizing events, and conflicts in other personality areas may cause frigidity.

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AUTHOR INDEX

August, 1949

- | | |
|-------------------------|------------------------|
| Abrams, R., 533 | Gonzalez, J., 557 |
| Acosta-Sison, H., 551 | Govan, A. D. T., 489 |
| Allgood, J. L., 478 | Greenblatt, R. B., 520 |
| Alter, M. M., 543 | |
| | Halpert, B., 565 |
| Barnes, J., 592 | Hamilton, J., 556 |
| Barns, H. H. F., 495 | Harrell, W. B., 550 |
| Barton, M., 588, 590 | Hartford, W. K., 565 |
| Bickers, W., 544 | Harvey, C., 589 |
| Black, M. G., 482 | Herzig, N., 459 |
| Brown, J. M., 481 | Heyman, A., 492 |
| Brown, R. C., 587 | Howson, J. Y., 547 |
| Burr, H. S., 546 | Huet, J. A., 600 |
| | |
| Caldwell, R. K., 497 | Ingraham, N. R., 490 |
| Calkins, L. A., 549 | Israel, S. L., 586 |
| Calvert, W., 506 | |
| Camello, A. A., 577 | Jackson, M. H., 589 |
| Carter, B., 574 | |
| Caton, W. L., 471 | Kaiser, I. H., 526 |
| Conrad, K. K., 479 | Kannapel, A. R., 486 |
| Counseller, V. S., 570 | Kao, H. L., 508 |
| Craig, S. E., 576 | Karsh, J., 499 |
| Cross, J. B., 492 | Kelso, J. W., 573 |
| Crossen, R. J., 580 | Kernodle, J. R., 529 |
| Cuyler, W. K., 529 | Knowlton, A. I., 488 |
| | Koch, M. L., 562 |
| da Paz, A. C., 591 | |
| Dearnley, G., 590 | Langman, L., 546 |
| de la Balze, F. A., 519 | Lascano, J. M., 557 |
| Delascio, D., 597 | Lawrence, R. F., 505 |
| de Moraes, A., 577 | Loeb, E. N., 488 |
| Dockerty, M. B., 538 | Lubin, S., 485 |
| Dodds, E. C., 595 | |
| Donato, V. N., 553, 557 | McCain, J. R., 492 |
| Dunlop, D. M., 493 | MacFarlane, C., 598 |
| | McGuff, P. E., 538 |
| Edmonds, D. G., 476 | McLane, C. M., 584 |
| Ellison, E. T., 550 | Massie, M., 544 |
| Evans, H. D., 486 | Mathews, R. A., 599 |
| | Mathiesen, K-M., 518 |
| Farell, D. M., 524 | Mathieu, J., 567 |
| Fowler, R., 577 | Medina, J., 601 |
| Frank, I. L., 564 | Mohler, R., 531 |
| Fulton, L. D., 487 | Monteiro, A., 555 |
| | Morgans, M. E., 495 |
| Gibson, J. G., 471 | |
| Gilbert, J. A. L., 493 | Nechtow, M. J., 533 |
| Gilmore, E. L., 534 | Nogués, A. E., 521 |

aside from the decrease in the number of the blood platelets, there are ecchymotic spots in the skin and hemorrhages occur in different mucous membranes and viscera. However, in these cases of metrorrhagia of puberty, even when thrombocytopenia is present, purpura hemorrhagica can be ruled out, since no signs of generalized vascular fragility are revealed and the bleeding and clotting times are within normal limits, as well as the contraction power of the clot. Hemophilia, therefore, can also be ruled out. It is the author's opinion that these forms of metrorrhagia of puberty can be explained by a sort of fragility affecting the vascular system of the uterus, especially of the endometrium, when uterine hypoplasia is present. It is possible that the estrogenic hormone, somehow altered in its chemical structure, acts as an irritant upon the vascular system of the uterus and as a toxic on the bone marrow, thus leading to metrorrhagia in the uterus and thrombocytopenia in the bone marrow. For that matter, there is experimental proof as well as clinical observations that estrogen may cause thrombocytopenia, agranulocytosis and aplastic anemia. The estrogenic hormone is normally secreted by the ovaries, but is probably altered at the level of the liver, due to an imperfect or defective metabolization. This is apt to occur when functional disturbances of the liver are present, perhaps due to deficiencies of vitamin B. There is clinical evidence that malnutrition may cause hypoplasia of the uterus and that patients with hepatic deficiency may show capillary fragility.

Nothing can be said regarding the pathology of these cases of pubertal bleeding with uterine hypoplasia, since curettage is almost impracticable in view of the presence of an intact hymen. As to treatment, anemia should be first removed with blood transfusions, liver extracts and iron. Bleeding can be temporarily stopped by radiation of the spleen. Vitamin B complex should be administered daily for a long period of time, and nutrition orders strictly observed. Every focus of infection should be removed. Estrogenic therapy should be resorted to for uterine hypoplasia later, after general conditions have improved.

(While it is true that drops in estrogen level are accepted as the cause of the bleeding phases in cases of the group discussed by the author, I do not believe that any such effect is thought to be mediated through the production of a uterine hypoplasia. While blood dyscrasias can undoubtedly explain some cases of pubertal bleeding, these cases constitute only a very small fraction, and accumulating evidence still supports the concept originally advanced by Schröder (1915) as regards these cases of metropathia hemorrhagica, as he called it. A better term would be anovulatory functional bleeding. Curettage is usually not indicated for diagnosis in cases of pubertal hemorrhage, but it is sometimes necessary for therapeutic reasons, as the quickest way to stop very profuse and often exsanguinating bleeding, with practically always preceding transfusions. The presence of an intact hymen is not a contraindication, and, for that matter, it is usually possible to perform the curettage without damaging the hymen. Finally, I believe that the author lays too much stress on vitamin B therapy, on the basis of the still very poorly established supposed hepato-ovarian syndrome, as discussed in the comment on the preceding abstract of the paper by Huet.—Ed.)

Reviews

NEW TOOLS FOR THE PHYSIOLOGIC STUDY OF HYPERTENSION IN THE TOXEMIA OF PREGNANCY

N. S. ASSALI*

Cincinnati, Ohio

It has been generally recognized that hypertension is one of the earliest and most constant signs of preeclamptic toxemia, and that it is caused by a generalized arteriolar vaso-constriction, (1, 2, 3, 4, 5, 6, 7, 8, 9). However, just what causes this arteriolar vaso-constriction is still an enigma. Many theories have been postulated but none of them has been supported by conclusive evidence.

Kellar and Sutherland (9) were the first to suggest that the elevation of the blood pressure in toxemia of pregnancy is due to chemical rather than nervous impulses. Their method of study, however, was subject to many variables and errors. Nevertheless, their ideas provoked much interest, and a search for pressor substances, hormones, enzymes, and enzyme inhibitors peculiar to gestation was initiated. Despite the fact that significant progress has been made, definite conclusions have not been reached.

During the last few years, new pharmacologic tools have been discovered and used for medical research in the field of hypertensive diseases. These tools have opened a new avenue of physiologic approach to the problem of hypertension in man. They advanced our understanding of the interrelated mechanism responsible for the maintenance of the blood pressure in health and disease. The object of this paper is to summarize our present knowledge of these tools and their application to a study of the specific hypertensive diseases of pregnancy.

TETRAETHYLAMMONIUM CHLORIDE (TEAC)

Acheson and Moe (10) were the first to note that this quaternary ammonium compound has the pharmacologic action of blocking the autonomic nervous system at the ganglionic level. The extension of this blockade is, as yet, not determined, but it is agreed that it involves the sympathetic and parasympathetic ganglia, (10-11) and is less complete than paravertebral block (13-14).

When this drug is given intravenously in standard doses to patients with hypertension of neurogenic origin, there is a marked fall in blood pressure to a level called "floor." This "floor" is supposed to be representing that portion of the blood pressure maintained by a humoral component, together with intrinsic tone inherent in the vessel walls. It has been shown that the depressor effect of TEAC is due to the blockade of sympathetic vaso-constrictor pathways to the arteriolar and possibly to the venous system (10-11-12-13-16-17). The drug has neither direct action on the vessel walls nor on the cardiac output (11-12). In

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- O'Brien, W. R., 599
 Osborn, S. B., 476

 Pacheco, U. M., 527
 Page, E. W., 487
 Park, W. W., 540
 Parker, R. T., 574
 Pillsbury, S., 483
 Potter, M. G., 502
 Purser, R. W. K., 568

 Quinlan, D. A., 541

 Rakoff, A. E., 523, 546
 Randall, L. M., 538
 Read, C. O., 575
 Reich, W. J., 533
 Reid, D. E., 471
 Ribeiro, P. B., 582
 Riley, C. L., 497
 Roby, C. C., 471
 Rocha, A. H., 530
 Rodrigues, F. V., 583
 Rouchy, M. R., 552
 Rudge, W. de S., 597
 Rydberg, E., 518, 536

 Sadugor, M. G., 502
 Sarrelangue, L. P., 562
 Sayhoun, P., 544
 Scheffey, L. C., 546
 Scott, J. M., 489
 Seegal, B. C., 488

 Senra, A., 542
 Sharman, A., 592
 Shotton, D. M., 503
 Siddall, R. S., 532
 Solth, K., 500
 Speiser, M. D., 554
 Still, R. J., 508
 Stoerk, H. C., 488
 Strassmann, E. O., 579
 Suran, R. R., 520
 Sutherland, A. M., 535
 Sutherland, B. M., 573

 Taylor, C. W., 503
 Taylor, H. C., 593
 Tennent, R. A., 540
 Terl6, L., 550
 Thomas, W. L., 574
 Torpin, R., 478, 481

 Volpitto, P. P., 481

 Waltman, R., 485
 Waugh, J. M., 538
 Way, S., 558, 566
 Weir, W. C., 572
 Wiesner, B. P., 588
 Word, B., 559
 Wright, H. P., 476
 Wurstner, T., 473
 Wyatt, J., 596

 Young, J., 568

its action on the hypertension is minimal and its effect is of short duration. Such side effects as tingling, tachycardia, and apprehension are of minor importance. Postural hypotension is very marked and should be carefully controlled. A certain amount of venous pooling is frequently observed, particularly in normal pregnancy. This possibly could be explained by the blockade of autonomic trans-

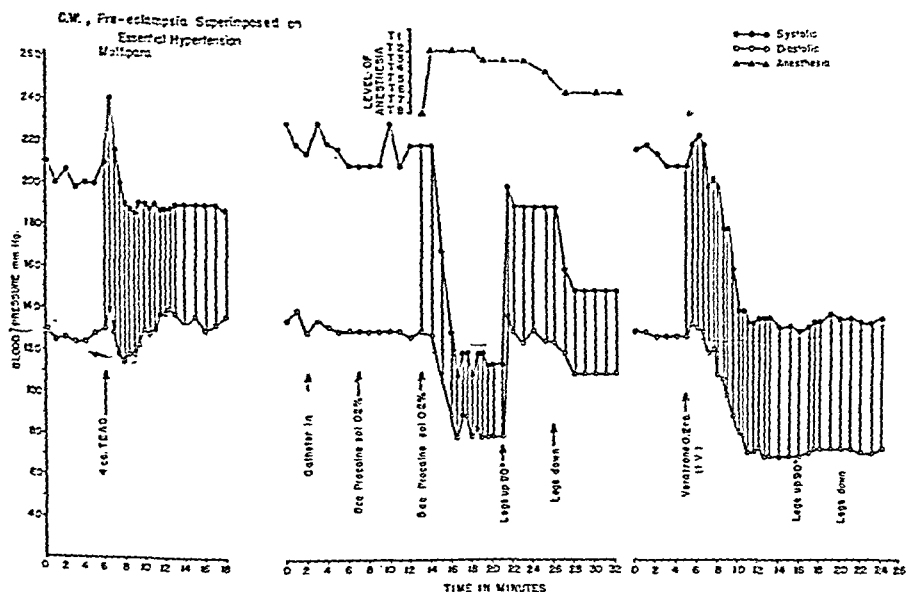


FIG. 2. Comparison of the effect of TEAC, high spinal anesthesia and veratrum on the hypertension of toxemia of pregnancy. This 29-year-old colored multipara had pre-eclampsia superimposed on essential hypertension. The diagnosis was based on the appearance of proteinuria, edema and further rise in the blood pressure during the last trimester of pregnancy. TEAC response was negligible. Spinal anesthesia produced a fall of 110 mm. of Hg. in the systolic and 50 mm. of Hg. in the diastolic blood pressure. Nausea, vomiting, and dizziness were prominent. Note the striking and sharp rise in the blood pressure when the legs were elevated 90°. The anesthetic level was maintained between T6 and T1.

Veratrum intravenously produced less fall in the systolic but a greater fall in the diastolic blood pressure than spinal. Consequently, the pulse pressure was wider. Again, nausea, vomiting and perspiration were present. Elevation of the legs at the height of veratrum effect did not change the blood pressure.

So far, this assay has been performed on 5 pre-eclamptic patients with uniform results.

mission to the venous system, aggravated by the weight of a heavy uterus upon the iliac vessels. TEAC may be used as a screening test in cases with borderline toxemia (16).

SPINAL ANESTHESIA

Another method of producing autonomic blockade of the vaso-constrictor fibers is by high spinal anesthesia. Some authors (11-13-14) believe that the blockade with high spinal anesthesia to include T4 is more complete than that

man this drug proved to be a valuable physiologic tool in the study of the mechanism involved in the maintenance of blood pressure. By the use of this drug, several authors (11-12-15) have demonstrated that elevation of the blood pressure in man could be due to either neurogenic or humoral impulses or both. The greater the neurogenic component of hypertension, the more marked is the effect of TEAC (11).

In this department, TEAC has been intensively studied either alone or in conjunction with veratrum viride and high spinal anesthesia in the pre- and postpartum periods of a large group of toxemic and normal pregnant patients (16-17). A standard test, which was described elsewhere (16), was used in all

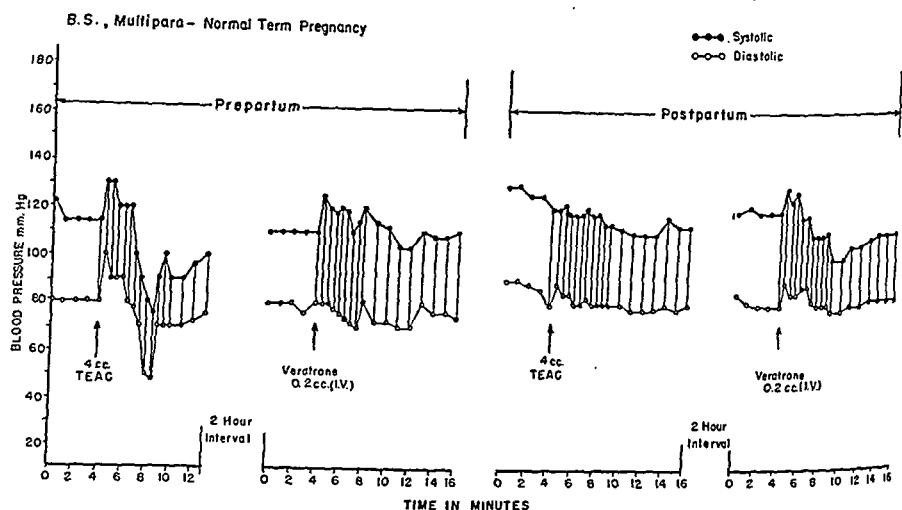


FIG. 1. Individual example where the effect of standard acute intravenous doses of TEAC¹ (400 mgs.) and veratrum viride (0.2 cc.) on the blood pressure of normal term pregnancy is compared. In the prepartum, TEAC produced a fall in the blood pressure to a floor of 75/48 mm. of Hg. The initial rise after the injection was supposed to be caused by extreme apprehension and anxiety due to the action of the drug. Veratrum response was not remarkable, despite the fact that bradycardia, nausea and vomiting were present.

In the postpartum, both TEAC and veratrum invoked negligible response.

patients. The results indicate that while in preeclampsia the blood pressure response to TEAC is negligible, in normal pregnancy, the blood pressure falls to a very low level (Fig. 1-2).

This further substantiates Kellar and Sutherland's (9) suggestion that toxemic hypertension is supported mainly by humoral agents, and that neurogenic impulses exert minor effects. The opposite occurs in normal pregnancy. It remains to be determined what the humoral factors are and where they originate. Page's study (18) on angiotonase and other enzymes, and Smith's work (19) on hormones and toxins may throw some light on these important questions.

TEAC is not a suitable drug for the treatment of toxemia of pregnancy since

¹ TEAC (Etamon) and veratrum viride (Veratrine) were supplied by Parke-Davis and Co., Detroit, Michigan, through the courtesy of Dr. E. C. Vonder Heide.

the necessity for further investigation. At the present time we are attempting to collect a larger series of cases where the effect of TEAC and high spinal anesthesia on the blood pressure and cardiac output of normal and toxemic patients is compared. The results will be the subject of further publication.

BENZODIOXANE—PIPERIDYLMETHYL BENZODIOXANE (933F)

This drug is a potent adrenolytic agent and it is valuable in differentiating between hypertension due to circulating epinephrine and other types of hypertension. Epinephrine may be increased in the circulation by certain epinephrine-producing tumors—e.g. Pheochromocytoma. Goldenberg, Snyder, and Aranow (30) have devised a standard method for testing such hypertensive patients with Benzodioxane. This drug is actually on trial in this department and as yet we have no conclusive evidence of its effect on toxemia of pregnancy.

DIBENAMINE (N,N-DIBENZYL-B-CHLOROETHYLAMINE) AND PRISCOL (2 BENZYLINDAZOLINE HYDROCHLORIDE)

These 2 compounds have almost similar pharmacodynamic properties and will be considered together. Both have sympatholytic and a slight adrenolytic activity. They block peripheral vaso-pressor reflexes not at the ganglia but at the nerve endings (31-32-33). Both produce marked side effects such as postural hypotension, nausea, vomiting, diarrhea, increased pilo-motor activity, etc.

The difference between the two drugs is that Dibenamine action lasts from 36 hours to 5 days and occasionally longer, whereas Priscol is of shorter duration. They have been used in human hypertension both for treatment and diagnostic purposes.

In this department, we have attempted to test toxemic patients with Dibenamine. Unfortunately, the undesirable side effects and many other difficulties have hampered our efforts and the experiments were discontinued. Both drugs, however, are still in our program for clinical and experimental investigation.

VERATRUM VIRIDE

This drug has been extensively used for years in this hospital in the treatment of toxemia of pregnancy (34-35-36). However, no quantitative measurement had been made of the fall in blood pressure following its use. Recently, a standard dosage and method have been devised for intravenous use of the drug (17). A group of toxemic and normal pregnant patients were tested in the pre- and postpartum periods. The results were reported elsewhere (17).

Veratrum viride proved to be a very effective and adequate drug in lowering the blood pressure in toxemia of pregnancy. Our findings demonstrate that the administration of a standard intravenous dose (0.2 cc.) of veratrum viride does not affect the blood pressure of normal pregnant patients, yet it invariably invokes a marked fall in the pre-eclamptic group. The depressor effect lasts for approximately one hour. This suggests a specific responsiveness of toxemic hypertension to the drug. Bradycardia, nausea, vomiting, and perspiration are frequently observed. They are not considered as toxic effects but rather as con-

with TEAC. Others (15) contend that for practical purposes they parallel each other.

The mechanism of fall of the blood pressure with high spinal anesthesia has been a debatable subject. Smith et al. (20) and others (21) have demonstrated that the hypotension is due mainly to capillary and venule dilatation, muscular paralyses, respiratory impairment, venous pooling, and decrease in the cardiac output. Others (22-23-24) have denied this.

In this department, clinical and experimental work with high spinal anesthesia was recently initiated, using a modified technic of Sarnoff and Arrowood (24-25). By this method, a low concentration of procaine (0.2%) can be used which permits the elevation of the anesthetic level up to T1, sometimes to C4 without seriously endangering the patient's life. At this level, the pinprick sensation and the vaso-constrictor fibers are supposed to be totally blocked while the motor fibers remain intact. Our small series indicates, so far, that a striking difference exists between the blocking effect of TEAC and high spinal anesthesia in toxemia of pregnancy. While TEAC produces a negligible drop in the blood pressure, high spinal invokes a marked fall with narrowing of the pulse pressure, marked venous congestion of the lower extremities, nausea and vomiting, apprehension, perspiration and other shock-like manifestations. The level at which the fall in the blood pressure begins is variable but it is usually between T6 and T1.

Why the effect on toxemic hypertension of sympathetic blockade with spinal anesthesia is different from that of TEAC is still a subject of speculation. Even accepting the fact demonstrated by Malton et al. (13) and Soloff et al. (14) that TEAC blockade is approximately 50 per cent less than spinal anesthesia, we still cannot explain the marked difference seen in toxemic pregnant patients. Alexandre and his co-workers (26) have demonstrated that some vaso-constrictor fibers may pass directly from the spine to the nerve without traversing the sympathetic ganglia. It is possible that spinal anesthesia blocks these fibers together with others and thus invokes more marked depressor effect than TEAC. The excessive venous pooling which is more strikingly observed with spinal anesthesia might also be a contributing factor. That this venous pooling is a major component of the hypotension of spinal anesthesia is evidenced by figure 2. When the patient's lower extremities were elevated 90° the blood pressure rose to almost its original levels. Since in our cases there was no motor paralysis, it must be admitted that venous blockade was responsible for the pooling.

Whitacre et al. (6-27) and Hingson et al. (28) have advocated the use of spinal anesthesia as a method of treatment of toxemia of pregnancy. Hingson (28-29) believes that it increases the urinary output and improves the cardiac condition of the patient by pooling a large amount of blood in the lower extremities. Smith and his co-workers (20) in their work have emphasized that the urinary output is never increased with spinal anesthesia and the pooling of blood in the lower extremities is an unphysiologic method of lowering the blood pressure. It is difficult to understand, on physiologic grounds, how such excessive pooling with impairment of venous return and auricular filling can be beneficial, except in rare cases. Nevertheless, the diversity of opinion on this subject points out clearly

hoped that with these pure substances, better drugs will be available for clinical and experimental studies.

Several other sympatholytic and adrenolytic agents, like F883, F1164, C5, dihydroergocornine, etc. have been developed and studied. They are omitted here for the sake of brevity and lack of personal experience with most of them.

V. W., Primipara—Severe pre-eclampsia

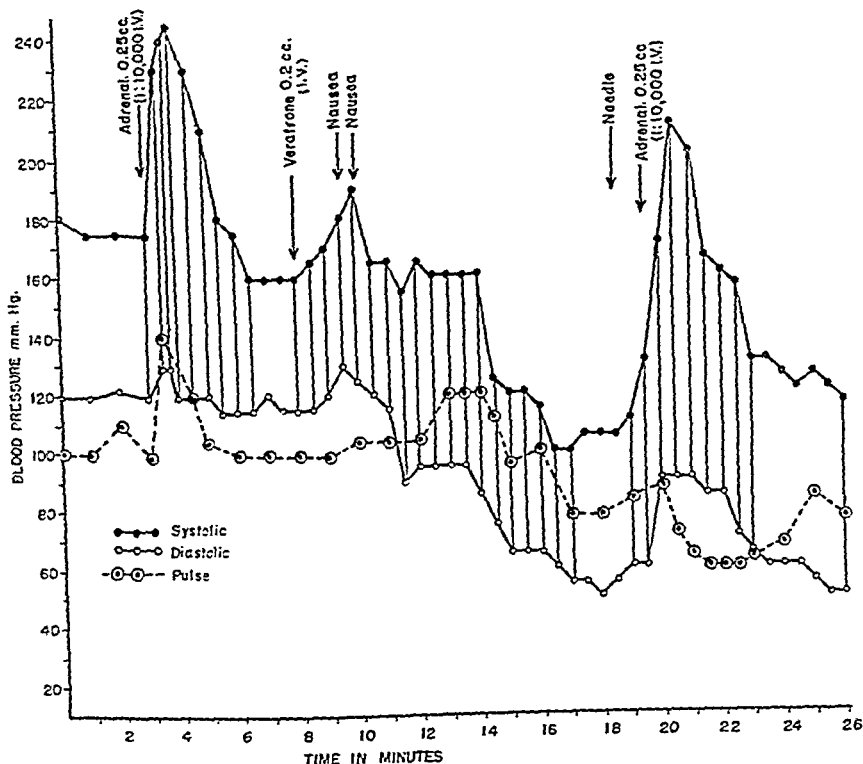


FIG. 4. Four pre-eclamptic patients were given adrenaline intravenously before veratrum administration and again at the height of veratrum effect. In toxemic patients, adrenaline invoked a marked rise in the systolic but a negligible response in the diastolic blood pressure. This case shows that there was no change between the first and second adrenaline response. Our results exclude entirely the possibility that veratrum viride acts by inactivating adrenaline or adrenaline-like substances.

SUMMARY AND CONCLUSION

New pharmacologic tools have been developed and used in the physiologic study of hypertensive diseases in man and animals.

The application of these tools to the study of specific hypertensive diseases of pregnancy may prove to be of value in investigating and detecting the nature of the blood pressure elevation and its origin. Furthermore, they may help in evaluating specific types of treatment.

comitant manifestations of the action of the drug. Transitory decrease in the urine volume may be observed, but it is harmless for the patient (37-38). Postural hypotension and venous pooling do not occur (17-43-44).

The pharmacology of *veratrum viride* has been extensively studied, but as a recent review (39) shows, there is no agreement as to its site of action. In animals, veratrum alkaloids act through a reflex mechanism in which the vagus nerve is involved (40-41). In man, it produces arteriolar vaso-dilatation without

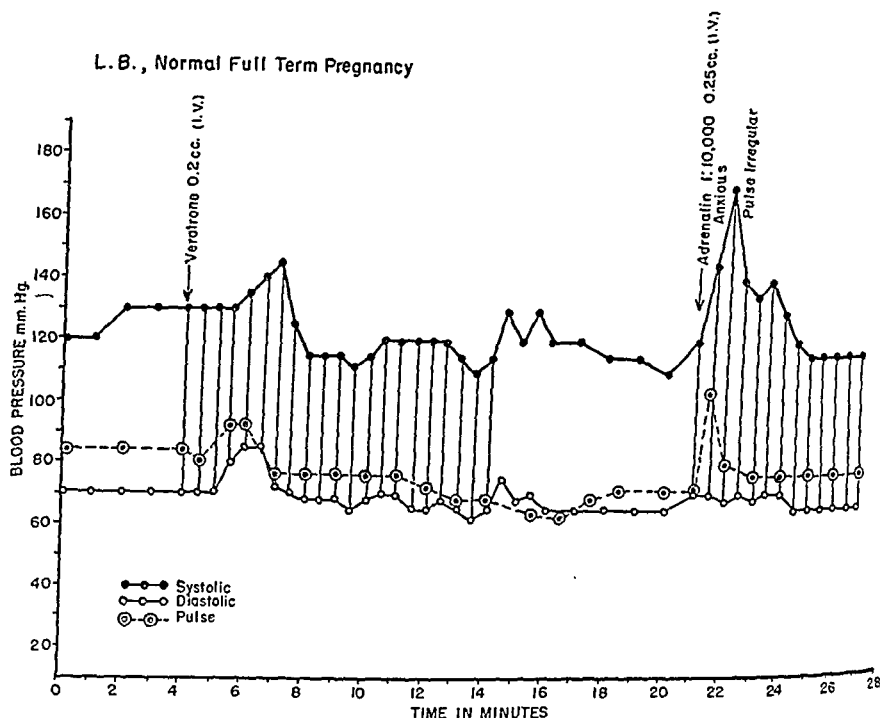


FIG. 3. An attempt was made to determine the site of action of *veratrum viride*. Adrenaline was given intravenously to 6 normal full term pregnancies, at the height of veratrum effect. This case illustrates that the adrenaline effect is not inhibited nor reversed by veratrum.

affecting the cardiac output (38). Furthermore, the drug does not act by inactivating adrenaline, since the response of "Veratronized" patients to intravenous administration of adrenaline is not changed (Figures 3-4). Likewise, the administration of atropin may abolish the bradycardia without affecting the hypotension (41-42).

At the present time there is an interest among several workers in obtaining pure veratrum alkaloids. Meilman and Krayner (44) have assayed protoveratrine and veratridine in animal and human hypertension. Protoveratrine invoked a marked depressor effect without producing any of the side effects of the crude veratrum preparation, whereas veratridine exerted an opposite action. It is

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was frequently found in cases of sterility. Artificial insemination was successful only when it was done when the cervical mucus presented these features. According to Moench (1934) the degree of penetrability of cervical mucus by spermatozoa seems to depend solely on the viscosity of the cervical secretion. Some of the findings of Séguy et al were confirmed by Wharton and Henriksen (1936) in their studies on ovulation with laparotomy observations at the time of intermenstrual pain. In 1937 Marshall and Hammond described a rough, subjective test for pregnancy in the cow based on recognition of the characteristic stickiness of the cervical secretion. Lamar, Shettles and Delfs (1940) and Shettles (1940) corroborated and extended the earlier French work. They observed that cervical mucus *in vitro* is easily penetrable during the menstrual flow but immediately afterward penetrability decreases. In only two of nine samples was there any evidence of penetrability between days 4 and 8 of the menstrual cycle. Twenty of twenty-nine samples tested from days 9 to 14 showed penetration, with maximal penetrability on days 14 and 15. During this optimal phase the rate of locomotion of the spermatozoa was two to three mm. per minute. With day 20 there began a phase of complete impenetrability which lasted until the onset of the menses. They concluded that the cervical mucus is most penetrable by spermatozoa at mid-cycle when it contains fewest leucocytes, is highly alkaline, is most abundant and possesses the lowest viscosity, at which time the spermatozoa may remain active longer in the mucus than in their own seminal plasma. This last conclusion was confirmed by Greenhill (1944) and Barton and Wiesner (1945a). Viergiver and Pommerenke (1944, 1946) obtained results in agreement with those of Séguy et al and Lamar et al. In addition, they weighed the average daily secretion of cervical mucus and found it to be about 60 mg., except during ovulation, when it may undergo a tenfold increase.

Rheology, the study of flow and deformation of matter, has played an important rôle in the investigation of cervical mucus during the estrus and menstrual cycles and pregnancy. In 1937 Blair designed an emptying capillary viscometer for the measurement of flow-elasticity or elastic recoil. When a material showing flow-elasticity is caused to flow along a tube, and the pressure is suddenly released, the material recoils back, towards its original position. Blair et al (1941, 1942) first observed this property in bovine cervical secretions, and that their viscous and elastic properties varied regularly during the estrus cycle. The viscosity reached minimum and flow-elasticity a marked maximum at the time of estrus.

Clift (1945) noted that the rate of flow of human cervical mucus is not constant at constant pressure. Accordingly, it is not a truly viscous fluid. He demonstrated two rheological properties of human cervical secretion, viz., flow-elasticity and *Spinnbarkeit*. *Spinnbarkeit* is the capacity of liquids to be drawn into threads. The emptying capillary viscometer of Blair was used to measure flow-elasticity. *Spinnbarkeit* was measured by drawing away a coverslip placed on a blob of mucus which was drawn out into a long thread, the length of which was measured. Flow elasticity and *Spinnbarkeit* were observed to undergo cyclic variation during the menstrual cycle and to bear relation to ovulation, to penetrability of cervical

CERVICAL MUCUS: CYCLIC VARIATIONS AND THEIR CLINICAL SIGNIFICANCE

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INTRODUCTION AND HISTORICAL

Many years before Sims invented the vaginal speculum, Robin (1848) noted the viscous nature of human cervical secretion, and in 1865 Smith concluded that conception is most likely "when the mucous contents of the cervix are in the most fluid condition." Sims first described the postcoital test, frequently called the Huhner test, in 1868 and emphasized that an important factor in its interpretation is the day of the menstrual cycle when the cervical contents are examined for the presence and condition of spermatozoa. He observed that the test is positive "when the cervical mucus becomes clear and translucent, and about the consistence of the white of egg—just before menstruation the cervical mucus is thick and opaque and almost sure to kill the spermatozoa."

It is now a definitely established fact that at the time of ovulation the cervical glands are markedly hyperactive, and there is then an increased exudate of lowered viscosity which permits greatest penetrability by the spermatozoa. At mid-cycle it is not unusual for patients themselves to report a clear, thin mucous discharge. This obtains often in women devoid of any cervical infection, including virgins. As will be shown in this paper, the cyclic variations in cervical mucus are another illustration of the remarkable integration of events to facilitate reproduction.

PHYSICAL PROPERTIES

Physiologic variations: The physical properties of cervical mucus are related to ovulation, to penetrability and longevity of spermatozoa, and to pregnancy. They undergo cyclic variation during the estrus and menstrual cycles. The study of Woodman and Hammond (1925) showed that during estrus, bovine cervical secretion is fairly fluid and capable of being drawn out into threads, whereas in diestrus, the mucus is less fluid; in pregnancy it is thick and adhesive. Séguy and Vimeux (1933) and Séguy and Simonnet (1933) observed that optimal conditions for penetrability of human spermatozoa obtain when the mucus of the cervical canal is abundant, fluid, transparent, and glairy. They postulated that these changes in the cervical mucus are associated with ovulation and likened them to the glairy, profuse, mucous discharge of subprimate mammals during estrus. They also correlated these changes with visual evidence of ovulation at laparotomy, maximal urinary estrogen level, and vaginal smear. In the average woman the stage of penetrability occurred in the middle of the cycle, beginning on day 10 of the menstrual cycle and lasting four or five days. An absence of such mucus

is tested *in vitro* against the ovulatory cervical mucus of a woman known to be fertile, and for testing the fertility of a woman, the receptivity of her cervical mucus is tested against the semen of a man of known fertility. The authors are of the opinion that both the invasion test of the mucus by the spermatozoa and the routine cytologic assay of the semen should be employed in the study of sterility in the male. Brewer and Jones (1947) used the changes in the cervical mucus as an aid in ascertaining the time of ovulation in women.

The cervical mucus cycle in fertile women is directly related to the basal body temperature. Viegner and Pommerenke (1944) and Pommerenke and Viegner (1946, 1947) investigated the relation between the amount of cervical mucus and the basal body temperature and found that the maximal secretion of mucus with lowest viscosity precedes the mid-cycle rise in temperature by one to three days. Barton and Wiesner (1945a) observed that the mucus increases in amount and becomes transparent just before the shift in temperature. After one to three days it decreases in quantity and again becomes cellular.

Experimental (Hormonal): A close connection exists between hormones and the nature of cervical mucus. Moricard (1936) gave 1 mg. of estradiol daily for 30 days to bilaterally oophorectomized women and observed an increased flow of clear, watery cervical mucus. In 1938 Sjövall reproduced the cycle in the cervical mucus in ovariectomized guinea pigs by the use of estrogen and progesterone. Watson (1939) observed patients who showed few actively motile spermatozoa at three successive postcoital examinations that were done at 48 hour intervals during the estimated fertile period. Each patient received 100,000 to 150,000 i.u. of estradiol benzoate intramuscularly, approximately 48 hours previous to the fourth postcoital test, at which time the cervical secretion was large in amount, transparent, low in viscosity, and contained many actively motile spermatozoa.

According to Sabine (1941) injection of estradiol benzoate, 0.2 mg., causes human cervical mucus to become transparent and liquid within a period of 24 hours. Progesterone, 10 mg., suppresses this effect.

Cervical mucus in menopausal patients both before and after estrogen therapy was studied by Shettles and Guttmacher (1940) and Guttmacher and Shettles (1940). Of twenty patients studied before therapy, all had scant cervical mucus with a pH of 4 to 5, highly viscous or crumbly in character, cloudy white or yellow with a heavy content of epithelial cells and leucocytes. In no instance was the mucus penetrable by spermatozoa *in vitro*. There was no demonstrable difference in specimens from cases of spontaneous and artificial menopause. These investigators found that by the administration of the proper dose of estrogens to these menopausal patients, readily demonstrable changes occur in the cervical mucus, until conditions typical of mid-cycle in the normally menstruating woman are achieved. They concluded that a study of the cervical mucus may prove an important guide for evaluation of estrogenic effects in the human.

In 1942 Bennett confirmed the findings of Shettles and Guttmacher and used their technique as one of four methods for the objective evaluation of estrogenic therapy in the menopause.

Pommerenke and Viegner (1946a) investigated five recently ovariectomized

mucus by spermatozoa and to pregnancy. Both were maximum at the time of ovulation when the mucus is thin, transparent, most penetrable by spermatozoa and favorable for their greatest longevity. *Spinnbarkeit* was almost absent in pregnancy. Clift states that penetrability of cervical mucus by spermatozoa probably depends on its molecular arrangement.

He reported that artificial insemination with semen mixed with white of egg is more successful than with semen alone. Since white of egg has rheological properties similar to those of mid-cycle cervical secretion, he recommends that cervical mucus from a fecund donor at the time of ovulation be used together with semen for artificial insemination. This recommendation is in view of the disappointing results of artificial insemination with semen alone in cases lacking suitable cervical secretion.

Plasticity, another rheological property and a characteristic of cervical mucus in pregnancy, is that property which enables a material to be deformed continuously and permanently without rupture. Clift applied a rheological law to cervical mucus, i.e., plasticity predominates in pregnancy and elasticity in non-pregnancy, especially at ovulation time. Blair diagnosed pregnancy in 96% of 155 samples by studying their plasticity and flow-elasticity.

Tack, a particular form of stickiness, is another rheological property of cervical mucus, seen to a marked degree only during pregnancy. It is measured by quickly drawing away a coverslip from a blob of mucus placed on a glass slide, during which the whole surface of the blob adheres to the coverslip and can be drawn only about one or two cm. away from the glass slide. Green (1941) invented a tackmeter for more exact measurement of this property.

Clift studied 143 samples of human cervical mucus at different stages of the menstrual cycle and during pregnancy, from the findings of which a rheological test for ovulation in women was formulated, i.e., the cervical mucus is more fluid, is homogeneously translucent, shows maximal elastic recoil and *Spinnbarkeit*, forms tough bubbles on homogenizing and has minimal cellular content.

A rheological test for pregnancy, demonstrable as early as the seventh week, is as follows: The cervical mucus is thick, homogeneously opaque, shows more or less absence of elastic recoil and *Spinnbarkeit*, does not form tough bubbles on homogenizing and tack is characteristically present.

According to Sims (1868) "in the investigation of a case of sterility—if we expect to proceed understandingly—we must determine whether the secretions of the cervical canal are favourable or not to the vitality of the spermatozoa." Lamar, Shettles and Delfs (1940) and Viergiver and Pommerenke (1944) recommend investigation of the cervical mucus throughout the cycle in cases of otherwise unexplained sterility. Guttmacher and Shettles (1940) selected the proper days for artificial insemination in humans from the character of the cervical mucus. Palmer and Marcille (1941) correlated the condition of the cervical mucus with infertility. Clift (1945) believes that the rheological phenomena and tests should prove of practical value in the recognition of ovulation and anovulatory cycles, in the investigation and treatment of cases of cervical hostility, as a tool in the study of ovarian dysfunction, and as an accessory test for pregnancy. Barton and Wiesner (1946) state that for testing the fertility of a man, his semen

marked at the third month. During the eighth month the cervix appears to be almost one mass of mucous tissue extending to the muscle layer. Wollner (1936, 1937) noted that after menstruation, as the cycle proceeds, the cells of the cervical mucosa bulge with secretion. McIlrath and Hellestrand (1948) reported that in cervical biopsies during the course of pregnancy secretory activity of the glands was evident at 4 to 5 months, very marked at 6 to 7 months. The glands were of many shapes, dilated and filled with secretion. These changes progressed to term. In confirmatory observations Fluhmann (1948) states that throughout pregnancy there is a marked production of mucus, especially after the twelfth week.

Atkinson, Shettles and Engle (1948, 1948a) studied histochemically the secretion of mucus by the human endocervix throughout the menstrual cycle in a series of cervixes removed surgically. They found that "relatively constant quantities of mucin are present in the apical cytoplasm of the cells of the glandular epithelium at all stages of the cycle. However, active secretion of this substance is a rhythmic process. Large amounts of mucin are liberated during the mid-cycle whereas relatively little secretion is found to occur during the late secretory, menstrual and early proliferative phases. In contrast to the normal cyclic cervix, little or no mucin is produced in the cervixes of postmenopausal women. During pregnancy, on the other hand, there is a marked increase in the amount of mucin present."

CHEMICAL PROPERTIES

Relatively few chemical studies have been made of cervical mucus. Woodman and Hammond (1925) found in bovine cervical mucus a mucoprotein belonging to the class of mucin bodies containing mucoitin sulphuric acid, since glucosamine was identified. In 1941 Blair pointed out that the total nitrogen in bovine cervical mucus reaches minimal values at about the time of estrus. In confirmatory experiments in 1946 by Boyland, the mucus at this phase of the estrus cycle was found to contain mainly carbohydrate. He believes that a mucopolysaccharide is possibly present in view of the study of Stacey in 1943. The mucus in estrus contained less protein and glucosamine than in diestrus and pregnancy.

The percentage of dry matter of bovine cervical mucus according to Blair (1941) reaches minimal values at the time of estrus. Boyland (1946) confirmed this and reported the dry matter to be 1.25% in estrus, 2.5% in diestrus and 4.5% in pregnancy. According to Pommerenke and Vieregger (1946) and Pommerenke (1947) human cervical mucus possesses its highest water content at mid-cycle with an average of 98% when the mucus is maximum in amount. No specimen of mucus contained less than 90% water.

Pommerenke (1947) and Vieregger and Pommerenke (1947) reported free reducing substances in cervical mucus in all phases of the menstrual cycle, with maximal concentration preceding and following mid-cycle. Hydrolysis gave additional quantities of reducing substances, about 50% of which were fermentable by yeast. Glycogen concentration underwent cyclic changes. When the maximal amount of cervical mucus at mid-cycle was considered, the maximum of reducing

women, four of whom also had subtotal hysterectomy, and confirmed Guttmacher and Shettles in their findings. They administered progesterone which produced no effect on the amount of cervical mucus secreted. Administration of alpha-estradiol benzoate and stilbesterol produced a significant increase in the amount and translucency of the mucus. Abarbanel (1946, 1946a, 1947, 1948) also confirmed the hormonal control of secretion by the cervix by the administration of estrogens to ovariectomized and subtotally hysterectomized women which produced copious, clear mucus of low viscosity. Then treatment with progesterone or ethinyl testosterone decreased the volume and increased the viscosity of the mucus secreted. In controls progesterone alone, as well as testosterone propionate and methyl testosterone, did not stimulate the flow of mucus.

ANTIBACTERIAL PROPERTIES

Cervical mucus seems to possess some antibacterial activity. In 1930 Goldsworthy and Florey investigated the antibacterial properties of mucus and their results are supported by those of Boyland (1946) in that remarkably little bacterial growth occurred in bovine cervical secretion kept alone or in water at room temperature. Beck (1942) states that the thick cervical mucus in the canal during pregnancy "aids in preventing the ascent of pathogenic bacteria into the uterine cavity." Barton and Wiesner (1945) observed that the mucus has bacteriostatic qualities, for agar plates with staphylococci may produce zones of inhibition when inoculated with cervical mucus. Pommerenke (1946) presented data suggesting inhibition of growth of certain strains of *Streptococcus hemolyticus* and *Staphylococcus aureus* and enhancement of growth of certain strains of *Neisseria gonorrhoeae in vitro* when cervical mucus was added to the culture medium. Koch (1947) correlated the growth of the gonococcus from cervical cultures with the phase of the menstrual cycle. Negative cultures were associated with the latter part of the luteal phase when the mucus was most acid, even though active foci of infection may be present deep in the cervical glands. Positive cultures were associated with the estrogenic phase when the pH of the cervical mucus was 6.8 and above.

Histological and Histochemical Changes

The secretion of cervical mucus has been studied histologically and histochemically. Stieve (1927) studied the histological changes which occur in the human cervix from the end of the second month of pregnancy until term. He found that the glands increase greatly in size with a corresponding decrease in the remaining interglandular substance. The cervical mucosa increases in thickness. A thick mucus is secreted from the enlarged glands which fills the cervical canal in its entirety. These changes progress with the duration of gestation. In 1935 Petrowa and Berkowskaja obtained sections of cervixes either at operation or parturition at varying times from 3½ to 9 months duration of pregnancy. They found that the cervical glands undergo increasing proliferation, hypersecretion and dilatation as pregnancy advances. Levey (1936) observed that mucus production in the cervix uteri occurs about the beginning of pregnancy and is very

though treatment with estrogens in appropriate doses results in the production of cervical secretion with all of its favorable characteristics, such therapy probably should be used with caution in an individual in whom these optimal changes do not appear, in view of the possibility of suppressed ovulation resulting. The physical and chemical characteristics of cervical mucus can be conveniently used as an additional index in evaluating the efficacy of estrogen therapy in the menopause. There is a high degree of correlation between relief of symptoms and the production of a thin, crystal-clear, readily penetrable cervical mucus by spermatozoa. Some menopausal patients make the same complaint as mentioned previously for women having normal menstrual cycles, of noting a clear, thin mucous discharge externally during the course of treatment with various estrogens. The changes in cervical mucus during pregnancy constitute another link in the reproductive chain, providing an antibacterial and mechanical barrier to the uterine cavity. The impenetrability of the cervical mucus during pregnancy by spermatozoa makes superfetation even a more unlikely possibility than it now appears. An important factor in the interpretation of results from cervical cultures for the gonococcus is the time of the menstrual cycle when the cultures are taken. Since negative cultures are associated with the latter part of the luteal phase of the menstrual cycle and positive with the estrogenic phase, they undoubtedly bear direct relation to the flare-up of pelvic inflammatory disease often seen following a menstrual period.

There are cases in which no deficiency can be established in either husband or wife and yet the marriage is sterile. An incompatibility between the semen and cervical mucus in some of these couples may be proven. The chemical analyses of the cervical mucus are considered a commencement in the elucidation of this problem.

Studies on the chemistry of the seminal plasma and spermatozoa are in progress. The changes in cervical mucus illustrate one of the many factors of importance in the study of sterility and reproduction.

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substances was also present, even though minimal concentration obtained at this time. The presence of tyrosine, tryptophane and cysteine and their contribution to the total amount of reducing substances were also noted.

In 1946 Boyland observed that bovine cervical mucus during estrus in the presence of 10 volumes of water may dissolve or swell to fill the total volume in 1 or 2 days at 15° C., while mucus obtained during diestrus and pregnancy remained discrete in water for many days. The three types of mucus are soluble in alkalis, concentrated mineral acid, neutral oxidizing agents (particularly sodium hypochlorite) and 1% solution of pancreatin, although mucus in pregnancy required 2 days for solution in the latter. Only that mucus obtained during estrus dissolved in takadiastase. None of the three types of mucus was altered by hyaluronidase.

The nature of polysaccharides in the translucent, acellular, mid-cycle human cervical mucus has been investigated by Shettles and Dische (1948). The total amount of true sugars varied between 0.120 and 0.250 per cent. Up to 22-35 per cent of the total carbohydrate calculated as glucose consisted of methylpentose and up to 55 per cent of galactose, according to methods of Dische and Shettles (1948, 1949). The rest was glucose. No significant amounts of hexoketoses, mannose or hexuronic acids were found. The ratio of galactose/methylpentose appears identical with that found in various preparations of blood group substances isolated from linings of stomach mucosa of hogs. The methylpentose and galactose of the mucus are precipitated by 90 per cent ethanol. These findings suggest that the main bulk of polysaccharides of human, mid-cycle mucus consists of a substance identical with or closely related to one of the blood group substances.

CLINICAL IMPLICATIONS

From the foregoing it can be seen that the changes in cervical mucus are of great clinical importance. As an aid in instructing patients concerning the time of the cycle giving the maximal possibility of conception, observations of the cervical mucus will be of distinct help. Also its changes can be utilized in timing ovulation and for artificial insemination. On the other hand, as a contraceptive measure, the characteristics of the cervical mucus can be ascertained and instruction given for those who practice rhythm as a birth control measure. In investigating sterility, one of the steps, as important as the diagnostic endometrial curettage, is to determine the presence of favorable or unfavorable cervical mucus at the time of ovulation. The simplest criteria for normal ovulatory cervical mucus are: pH, gross appearance, amount (range), and viscosity by simple cover-glass test, which can also be observed at time of the post-coital test. If the normal changes do not occur, then an infected or abnormally secreting cervix may warrant treatment. Ovulatory cervical mucus of a woman known to be fertile may be used to test *in vitro* the semen of a questionably fertile man. Changes in the characteristics of cervical mucus during the cycle are hormonally controlled and correlate well with cyclic changes in endometrial histology, vaginal smears, appearance of ovary at laparotomy, and basal body temperature. Even

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and forms of treatment may provide a clue as to the pathogenesis of habitual abortion.

(In the welter of articles on the treatment of habitual abortion, the above contribution is noteworthy for a number of reasons. In the first place, it is a controlled investigation including a group of patients with no therapy, a group in which progesterone was administered, and still a third in which no steroid hormones were used but simply nutritional guidance, psychotherapy and thyroid extract when the basal metabolic rate was low. Secondly, with the exception of the secondary group given Type III therapy, the number of patients in each category is large enough to permit of fairly valid conclusions. Thirdly, the study deserves attention because of the striking outcome, namely, optimal results in the group which was given no steroid hormones but simply general nutritional and hygienic measures plus thyroid when indicated. The 80 per cent salvage rate reported in the primary abortion group with Type III therapy is not only good when compared to the 2 other primary abortion categories, but can easily stand comparison with the best figures which have hitherto been recorded as the result of any method of therapy.

The results reported by Javert are somewhat similar to those obtained by Delfs and Jones in our own Clinic. These authors, using the same definition of habitual abortion as does Javert, made careful evaluation of patients from the viewpoint of various deficiencies: thyroid, progesterone, serum chorionic gonadotrophin, vitamin E, etc., and administered therapy only when such deficiencies were demonstrable. In 43 pregnancies occurring in 39 women, Delfs and Jones obtained living infants in 67.4 per cent of the cases. Their data indicate that deficiency of progesterone alone is rare. Even when associated with other deficiencies only 17 per cent of the successfully treated cases had any indication for progesterone therapy. Of the cases ending in abortion, 7 or 50 per cent showed low pregnanediol, but over half of these were not salvable as they had defective pregnancies when first seen. They believe that progesterone is desirable for the few cases which are deficient but that it alone cannot be expected to benefit the larger number which have no deficiency. However, when facilities for pregnanediol determinations are lacking, progesterone therapy, in their opinion, may be given with no harm and occasional benefit. Delfs and Jones believe that the most logical use of progesterone in habitual abortion, when trouble may be anticipated, would seem to be prophylactic treatment in the premenstrual period and through the early weeks of pregnancy as suggested by Rutherford (*Am. J. Obst. & Gynec.*, 1946, 51: 652). In their opinion low thyroid function is by far the most common deficiency encountered in habitual abortion as it occurred in 31 cases or 72 per cent of their series of 43 cases and was the sole factor in 19 or 44 per cent.

The attitude of Javert toward progesterone in the management of habitual abortion is still less favorable than that of Delfs and Jones since he finds that it can be eliminated with out any noticeable reduction in full term fetal salvage. Although the problem is by no means settled, studies such as the above and that of Delfs and Jones make us ponder just how important progesterone and estrogen therapy actually is in the treatment of this condition. —Ed.)

ECTOPIC PREGNANCY

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Am. J. Surg. 77, 273, 1949

Ectopic pregnancy is broadly defined as the existence of an embryo or fetus outside the uterine cavity; the terms ectopic and extrauterine may be used interchangeably.

Obstetrics

PATHOLOGY OF PREGNANCY

HABITUAL ABORTION

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N. Y. State J. M., 48, 2595, 1948.

Primary habitual abortion designates the obstetric problem of patients who have had 3 or more consecutive spontaneous abortions in the first 3 pregnancies. Secondary habitual abortion indicates those patients who have had 3 or more consecutive abortions after one or more immature, premature, or full-term infants. An abortion is defined as the termination of pregnancy at 22 weeks or less with the fetus weighing 500 gms. or less.

Over a 15-year period, the incidence of primary habitual abortion was 1 in 300; that of the secondary type 1 in 493. There were 123 patients in the primary group who had 669 pregnancies, and 88 secondary abortion patients who had 679 pregnancies, a total of 1,348.

Treatment of the patients was of 3 types. Type I received no treatment. There were 189 pregnancies in the primary habitual abortion patients and 161 in the secondary group. Type II were treated with bed rest, sedation, Vitamin E, progesterone, and occasionally arsenicals. There were 50 primary and 41 secondary abortion pregnancies in this group. Type III received nutritional guidance, dietary supplements with vitamins C, K, and minerals, thyroid extract when the basal metabolic rate was low, and psychotherapy. There were 41 primary and 7 secondary abortion pregnancies in this group.

The percentage of full-term infants in the primary group was 26 with Type I therapy, 64 with Type II therapy, and 80 with Type III therapy. In the secondary group 48% of the patients with Type I therapy had full-term infants; 48% with Type II therapy and 100% with Type III therapy had full-term infants.

Spontaneous delivery occurred in most of the patients. Normal delivery occurred in 68% of the primary group and in 88% of the secondary group. Congenital anomalies were present in only 4 infants. Three maternal deaths occurred following operative delivery.

Current treatment consists of nutritional instructions, dietary supplements including vitamins C and K and minerals, psychotherapy, prohibition of mineral oil, use of thyroid extract when the basal metabolic rate is low, interdiction of intercourse during the entire pregnancy, and removal of all gynecologic defects. Elimination of vitamin E and K and progesterone has produced no noticeable reduction in full-term salvage. Gradual elimination of various agents, methods

pregnancy include severe abdominal pain, nausea, vaginal bleeding and shock. A pelvic mass is often present. On the other hand, diagnostic errors are very common in the atypical case, particularly if the gestation is unruptured. Amenorrhea, pain upon motion of the cervix, presence of a pelvic mass and vaginal bleeding are important features. The latter usually does not occur prior to the death of the fetus.

Amenorrhea occurred in 73% of the 173 cases studied by the author. Abdominal pain was present in 88.4%. Pain generally occurred after exertion, coitus or defecation. The pain of unruptured tubal pregnancies is usually secondary to distention of the broad ligament structures; rupture of the gestational sac is accompanied by severe pain resulting from the tearing of the tube and the irritation of blood in the peritoneal cavity. Vaginal bleeding or spotting occurred in 73% of the cases studied. Nausea and vomiting occurred in 32% of the author's cases, faintness and weakness in 47%, shock in 9.2% and urinary symptoms in 6.4%. Breast changes, rectal tenesmus and constipation were other more infrequent symptoms.

Abdominal tenderness and rigidity occurred in 48% of the author's cases, abdominal mass in 7.5%, tenderness on motion of the cervix in 29.5% and pelvic mass in 51.4%. The masses varied in size, consistency and position, depending upon the age of the pregnancy and the extent of the hemorrhage. The passage of a decidual cast is of great diagnostic value but does not often occur.

In abdominal gestation, there may be an early history suggesting tubal rupture. If the fetus survives and grows, symptoms of peritoneal irritation may become very marked, particularly after the 5th month of pregnancy. At term spurious labor may occur. In an advanced abdominal pregnancy, the uterus may reach the size of a 4-month pregnancy. The fetus will be readily palpable beneath the abdominal wall. X-ray may show that the fetus is not in the uterus.

Ovarian pregnancy has the same symptoms as tubal gestation. Rupture with severe hemorrhage tends to occur about the 6th to 8th week.

Cervical pregnancy is marked by hemorrhagic vaginal discharge which is usually painless. If the fetus is more than 12 weeks old, the gestation sac may sometimes be identifiable from below.

In this series, the Friedman test was positive in 43 of the 53 cases in which it was done. Puncture of the pouch of Douglas with a needle of large bore is advocated by many authors who regard the presence of old clotted blood as significant. Colpotomy may differentiate the condition from pelvic abscess. Curettage is of doubtful value.

In this series 91.9% of the cases were correctly diagnosed prior to operation. Confusion most often occurs with appendicitis, salpingitis, ovarian cyst and incomplete abortion. Diagnosis is most often obscure when the tube is not ruptured. Angular pregnancy, corpus luteum rupture, corpus luteum cysts, twisted ovarian cysts, myomata, and ruptured Graafian follicles may also obscure the condition.

In 52% of the cases, the tubal pregnancy occurred on the right side, in 42% on the left side and 0.6% bilaterally. In 5.2% the pregnancy was abdominal. In the tube, the ampulla is the favorite site of nidation. The isthmus, infundib-

Historically ectopic pregnancy is described in the Talmud, by the Buddhists and the Arabians. The earliest extrauterine pregnancies to be recognized were those which went to full term or were retained as lithopedions. Many of the earliest successful cesarean sections were crude laparotomies for the removal of secondary abdominal pregnancies.

The first American operation for ruptured ectopic pregnancy was performed by Briddon in 1883. In the same year Lawson Tait became the first to operate successfully for ruptured tubal pregnancy.

True ectopic gestation in animals is extremely rare but has been described in cattle, swine, rabbits, sheep and dogs, as well as anthropoid apes. Most of these pregnancies are abdominal, but a few are true tubal gestations.

The author studied ectopic pregnancies occurring in the Sydenham Hospital from 1934-1947. In this series, one ectopic pregnancy occurred for every 69 intrauterine pregnancies and one for every 44 gynecological admissions. The greatest number of extrauterine gestations occurred in the 5-year period from 26 to 30 years of age. The majority of the patients had had at least one previous pregnancy.

The 4 types of ectopic gestation in order of frequency are (1) tubal, (2) abdominal, (3) ovarian, and (4) cervical. The first type is caused by some factor which prevents the fertilized ovum from reaching the uterus. In many cases this factor is the result of previous pelvic inflammatory disease. The latter may act by causing thickening of the tubal walls, interfering with the tubal peristalsis, preventing tubal ciliary activity or by causing mechanical obstruction of the tube. In 129 tubal pregnancies, the author found salpingitis in 52.8%. The pelvic inflammation is frequently gonorrheal but may be the result of previous abortion or peritonitis. Numerous authors have observed that women who have had pelvic inflammatory disease followed by a period of sterility may develop ectopic pregnancy. On the other hand, many authors feel that inflammatory disease of the uterus and tubes should be disregarded as causative factors in ectopic gestation. Litzenberg could find positive evidence in less than 10% of his cases. Ectopic gestation occurs more frequently in urban areas. The author feels that this is further evidence that pelvic inflammatory disease is a cause of this abnormality.

Salpingitis, tubal adhesions, previous abdominal and pelvic operations, neoplasms, congenital malformations of the tube, abnormal ova and tubal atrophy may cause tubal pregnancy. If the tube be atretic or occluded, external migration may occur. The formation of decidua in areas of tubal endometriosis, tubal spasm, metabolic deficiency and intrauterine pessaries has also been suggested as causes of tubal pregnancy.

Most abdominal pregnancies are secondary as the result of rupture of the tube. Primary abdominal pregnancies have undoubtedly occurred, and may be associated with the increased incidence of pelvic endometriosis.

Ovarian pregnancy may result from primary or secondary implantation in the ovary; in cervical pregnancy, the ovum traverses the entire uterine cavity and lodges in the cervix before implanting.

The symptoms and physical findings of the typical victim of ruptured tubal

in the treatment of ectopic gestation. In the author's series, 73.4% of the patients received either transfusion or intravenous infusion during or after the operation. Before the abdomen is opened, a needle should be introduced in the vein to keep it patent, but active infusion should be deferred until the abdomen is opened and the bleeding vessels clamped. The larger blood clots should be removed; free blood in the abdominal cavity may be left in situ.

In tubal pregnancy, the whole tube, including the interstitial portion, should be removed. However, if the woman is childless and the other tube has been removed, as much as possible of the proximal portion should be saved. The author prefers the abdominal route to vaginal section; vaginal section restricts the operative field and there is always a possibility that the operation cannot be completed by the vaginal route. In early interstitial gestations, cornual resection with conservation of the uterus may be performed. In cases of interstitial pregnancy which have progressed beyond 5 months, supra-vaginal hysterectomy is the wisest procedure.

Pelvic hematocele should be treated surgically—by laparotomy if blood is present, by colpotomy if pus is found.

Early abdominal pregnancy should be terminated by prompt laparotomy. The treatment of advanced abdominal pregnancy presents major problems in the management of sac, adhesions, placenta, and in the control of hemorrhage.

The treatment for ovarian pregnancy is ovariectomy as soon as the diagnosis is made. The products of most cervical gestations can be removed per vaginam. If the pregnancy has advanced beyond the 4th month, total hysterectomy may be the safer procedure.

Postoperative complications were present in 17 patients (9.8%). There were 5 deaths, a mortality rate of 2.9%. Death resulted from paralytic ileus, hepatorenal syndrome, peritonitis and in 2 instances hemorrhage. Reduction of mortality in ectopic pregnancy depends upon correct early diagnosis, immediate preoperative treatment of shock, careful choice of anesthesia, prompt operation, adequate blood transfusions, administration of antibiotics, and postoperative treatment. Reduction of mortality in abdominal pregnancy largely depends upon early diagnosis, judicious management of the placenta and free use of blood transfusions.

(These 2 articles by Jarcho constitute one of the best surveys of ectopic pregnancy to appear in many years. Since they are themselves largely collective reviews, they do not lend themselves to further condensation and only a few salient points have been included in the above abstracts. These 2 articles together make a small monograph of 83 pages.

In this year of 1949, which marks the fiftieth anniversary of Lawson Tait's death (June 13, 1899), Jarcho's comprehensive historical introduction is appropriate as well as interesting. As might be expected, the first type of ectopic pregnancy to attract notice was full term abdominal pregnancy and most of the very early operations were for that condition. As Jarcho recalls, the first full operation for extrauterine pregnancy in the United States was the famous and successful case of Dr. John Bard of New York described in a letter to Dr. John Fothergill of London and by him communicated to the Society of Physicians in London (Medical Observations and Inquiries by a Society of Physicians in London, 1764, II, pp. 369-372). The patient was a certain Mrs. Stagg, the wife of a mason. Her first

ulum and interstitial portions follow in order of frequency. Decidual formation in the tube is imperfect; the ovum implants in a manner similar to that seen in a normal pregnancy. The ovum accordingly penetrates large vessels in the tubal muscularis with intraperitoneal bleeding. The capsule of the pregnancy may rupture producing a "tubal abortion." Finally the tube may rupture.

When nidation occurs in the ampulla, the pregnancy usually terminates in tubal abortion. Isthmic and interstitial pregnancies usually rupture. The latter ruptures late and such a rupture may be most disastrous.

Ovarian pregnancy cannot be diagnosed unless (1) the tube is intact, (2) the gestation sac occupies the position of the ovary, (3) the sac is connected with the uterus by the ovarian ligament, (4) definite ovarian tissue is found in the wall of the sac. About 60 authentic cases appear in the literature.

In the opinion of the author, primary abdominal pregnancy is more likely to occur in the presence of endometriosis. To prove a primary peritoneal pregnancy, both tubes and ovaries must be normal, there must be no evidence of a uteroperitoneal fistula and the pregnancy must be related exclusively to the peritoneal surface and be young enough to obviate the possibility of a secondary peritoneal nidation.

Cervical pregnancy may not be diagnosed unless (1) there are cervical glands opposite the placental attachment, (2) the placenta is intimately attached to the cervix, (3) the placenta is situated below the entrance of the uterine vessels or the peritoneal reflections on the uterus, (4) fetal parts are not present in the uterus.

Combined intra- and extrauterine pregnancy may occur simultaneously or one pregnancy may be superimposed upon the other. Recurrent ectopic pregnancy is said to occur in 3-5% of the cases. A normal intrauterine pregnancy may sometimes intervene between 2 ectopic gestations.

(See editorial note appended to following abstract.—Ed.)

ECTOPIC PREGNANCY II. WITH SPECIAL REFERENCE TO ABDOMINAL PREGNANCY

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Am. J. Surg. 77, 423, 1949

Every case diagnosed as ectopic gestation requires surgical treatment. When the clinical picture indicates an intact ectopic gestation, immediate laparotomy should be performed. When the patient's condition is precarious and the diagnosis is questionable, preoperative treatment is instituted and operation performed as soon as there is improvement in the volume of pulse and systolic blood pressure. The author used cyclopropane in his series.

Whole blood, plasma and solutions of salt and glucose are indispensable aids

make at once for the source of the haemorrhage, the broad ligament, tie it at its base, and then remove the ovum, debris, and clots at leisure."

Less than 3 months later Tait was called in consultation by a certain Dr. Page of Solihull to see still another similar case. Tait ligatured the ruptured tube and broad ligament and this woman was the first ever to survive operation for the rupture of a tubal pregnancy.

The fiftieth anniversary of Tait's death has been marked by a new biography of this colorful figure, who was at once the Father of British Gynecology and a perennial storm center for all kinds of invective, law suits and malicious gossip. The author, Dr. I. Harvey Flack, recounts Tait's ups and downs and his many tribulations in fascinating detail (Heinemann, London, 1949).

But to return to Jarcho's papers, one of the unique sections is that dealing with the comparative anatomy of ectopic gestation in which he points out, with veterinary documentation, that ectopic gestation is extremely rare in the lower animals. He believes that this difference is attributable to our complex social order which has created certain common causes of tubal gestation such as gonorrheal salpingitis and abortion.

The section on the important matter of signs, symptoms and diagnosis is exceptionally full and instructive and the many illustrations are especially informative.

The figure of 3 to 5 per cent for the incidence of recurrence of ectopic pregnancy is in keeping with general experience but unless the reader understands fully what is meant, it may prove misleading. Actually, because of the bilateral character of most of the conditions which predispose to ectopic pregnancy, sterility is frequent after operations for this condition and even in women who are left theoretically fertile, the incidence of further conception is less than one in three. Now, among these women who actually become pregnant after previous ectopic gestation, the incidence of another extrauterine pregnancy ranges from 10 to 15 per cent in various reports. In other words, among pregnancy subsequent to an ectopic gestation, one pregnancy in 7 to 10 is again extrauterine. Nevertheless, the overall figure of 3 to 5 per cent is valid because it refers simply to the frequency of subsequent ectopic pregnancy among all women who have had a previous extrauterine gestation whether they subsequently become pregnant or not. This difference in calculating the incidence of recurrent ectopics may impress some readers as inconsequential, but it does throw a somewhat graver light on the gestations which actually occur after this complication.

In sum, Dr. Jarcho is to be congratulated on this comprehensive and scholarly review of one of the most important complications in our specialty.—Ed.)

UTERINE PROLAPSE IN SECOND TRIMESTER OF PREGNANCY SUCCESSFUL TREATMENT OF A CASE

THEODORE F. HAWKINS

Dept. of Obstetrics and Gynecology, Mercy Hospital, Philadelphia, Pa.

Pennsylvania M. J., 52: 604, 1949.

Prolapse of the uterus is unusual after the 4th or 5th month of pregnancy because the uterus rises high out of the pelvis. Five cases have been reported in which prolapse occurred between the 4th and the 8th months. None of these cases went to term. Pregnancy, at or near term, associated with prolapse of the uterus has been reported 203 times in the literature.

Most authorities agree that if prolapse occurs during pregnancy, some method

pregnancy was perfectly normal; the second, however, ended in false labor at term, after which a distinct tumor remained in the abdomen. Five months later she conceived again and after a short and easy labor gave birth to a living child at term. Subsequently the patient suffered from fever and diarrhea, and the abdominal tumor became painful and gradually increased in size, so that at the end of 9 weeks definite fluctuation could be detected. The patient was then seen in consultation by Dr. Huff, an Army surgeon, when he and Bard made a positive diagnosis of extrauterine pregnancy and later determined to operate. Upon opening the abdomen a large amount of fetid pus escaped from the tumor, after which a macerated fetus was removed, but no trace of a placenta could be found. The wound was treated by the open method, healed in 6 weeks and the patient made a complete recovery.

By stretching the meaning of the term "operation" a little, it can be said that Gloucester, Massachusetts can claim an even earlier operative intervention for extrauterine pregnancy. It is reported in the *American Magazine*, Boston, 1746, and is reproduced in an article by Dr. George Osgood: "A Remarkable Extrauterine Case." (*Medical Communications to the Massachusetts Medical Society*, Boston, 1790-1808, I, No. 2, Part II, pp. 30-41). The patient was a certain Mrs. Low of Gloucester. Her second pregnancy ended in a false labor, leaving behind an abdominal tumor which she carried with her for 16 years. During this period she gave birth to 6 other children and after the delivery of the last one on March 5, 1745, she was taken ill with chills, high fever and abdominal pain. A little later an opening appeared in the abdominal wall over the tumor, through which pus was discharged. This gradually became larger, and eventually a number of small bones were passed through it; and on introducing the finger into the fistulous tract the head of the child could be distinctly felt. "On June 24, in the presence of the Reverend John Lowell and the doctor's 2 sons, an incision was made and the rest of the bones extracted daily until the 28th, when the last were taken away and the wound stitched up." The patient died 4 days later and at autopsy it was found that the fetus was contained in the left tube, while the right tube and ovary, as well as the uterus, were perfectly normal. The name of the operator is not given.

The cases of Tait and Briddon were apparently the first abdominal operations performed for classical rupture of an early tubal pregnancy with massive abdominal hemorrhage. Tait's well known pioneer work in the operative treatment of ruptured tubal pregnancy, stemmed from trial and error. As described in his own words:

"In the summer of 1881, I was asked by Mr. Hallwright to see with him in consultation a patient who had arrived by train from London in a condition of serious illness, that illness having been diagnosed by Mr. Hallwright as probably haemorrhage into the peritoneal cavity from a ruptured tubal pregnancy. The patient was blanched and collapsed, the uterus was fixed by a doughy mass in the pelvis and there was clearly a considerable amount of effusion in the peritoneum but no distinct tumor could be felt above, and I agreed with Mr. Hallwright as to the nature of the lesion. This gentleman made the bold suggestion that I should open the abdomen and remove the ruptured tube. This suggestion staggered me, and I am ashamed to have to say I did not receive it favorably. I saw the patient again in consultation with Mr. Hallwright and Dr. James Johnson and again I declined to act upon Mr. Hallwright's request, and a further haemorrhage killed the patient. A postmortem examination revealed the perfect accuracy of the diagnosis. I carefully injected the specimen which was removed, and I found that if I had tied the broad ligament and removed the ruptured tube I should have completely arrested the haemorrhage, and I now believed that had I done this the patient's life would have been saved."

On January 17, 1883, Lawson Tait performed the first abdominal operation for ruptured tubal pregnancy but this patient also died. He was convinced, however, that the death was the result of certain technical errors which he had made and as a result he formulated what seemed to him a more rational operative program in such cases, as follows:

"But my conclusion was speedily arrived at, that I had blundered—that the true method of operating on such a case was to separate adhesions rapidly, regardless of bleeding, and

THE TREATMENT OF LYMPHOGRANULOMA VENEREUM AND GRANULOMA INGUINALE IN HUMANS WITH AUREOMYCIN

L. T. WRIGHT, M. SANDERS, M. A. LOGAN, A. PRIGOT AND L. M. HILL

Harlem Hospital and Columbia University, New York, N. Y.

Ann. New York Acad. Sc., 51: 319-330, (Nov.) 1948.

The writers present 10 new cases of lymphogranuloma venereum which were treated with aureomycin and review 25 cases of the same disease previously reported. The treatment in all of these cases has consisted of 10 to 40 mg. of aureomycin daily, given intramuscularly with the exception of 2 cases in whom larger doses were given orally. The duration of treatment has been determined by the clinical course. The results obtained in these patients have been excellent, and both the buboes and the proctitis show rapid improvement after the drug is given. In those cases in which rectal strictures have developed, no essential change in the degree of stricture could be noted after the use of aureomycin, but secondary infections usually encountered were kept under control by the drug. It is concluded that aureomycin is a superior specific form of therapy for the lymphogranuloma venereum virus.

Fourteen of the original 25 cases reported in the authors' previous paper have now been followed for periods of time varying between 2 and 16 weeks after discharge from the hospital. These cases show that the curative effects of aureomycin persist after the treatment has been stopped.

Three cases of granuloma inguinale in whom ulcerative lesions were present were treated with aureomycin. The dosage varied between 560 mg. given intramuscularly to one patient and 75.6 gms. given orally in another case. The lesions had been present 4 months in the first patient, 7 years in the second, and 10 years in the third patient. All 3 of these patients showed rapid healing of the ulcer and the first patient was felt to be entirely cleared. The lack of toxicity in the dosage used and the fact that it can be used orally demands further study of aureomycin in lymphogranuloma venereum and granuloma inguinale.

(Obstetricians who have to do with the management of colored patients will welcome any new agent which proves effective against lymphogranuloma venereum because a frequent aftermath of this disease, rectal stricture, is such a potential handicap in child-bearing. Prior to the introduction of aureomycin, there was no cure for this condition and its ravages in the rectum and rectovaginal septum were often extensive. It appears to be true, as the above abstract indicates, that rectal strictures do not disappear with this treatment, but it is nevertheless to be hoped that in the future early therapy will decrease their frequency and degree.—Ed.)

should be used to hold the uterus up until after the 5th month, when it should stay up of itself.

The author reports the case of a 20 year old gravida iv, para 3, who presented herself at 7 months gestation with prolapse of the uterus. The entire cervix and a portion of the lower uterine segment protruded from the vagina. The uterus was replaced and the patient fitted with a stem pessary and belt. The pessary remained in place for 6 weeks and was then removed. The patient went to term and was delivered of a living 8 lb. 8 oz. infant. No recurrence of the prolapse took place after removal of the pessary and belt. Later a combined plastic and abdominal operative procedure was carried out.

This is the 2nd case in which a living baby has been obtained from a prolapse of the uterus occurring so late in pregnancy.

EXTRAMEMBRANOUS PREGNANCY

MARY K. LAWLOR

Proc. Roy. Soc. Med., Lond., 42: 64, 1949.

The author reports one case of extramembranous pregnancy. The patient was admitted to the hospital with symptoms of threatened miscarriage at 10, 14, 21 and 24 weeks. At 30 weeks, the patient was admitted with blood-stained discharge. Diagnosis of placenta previa and threatened premature labor was made. The uterus was smaller than that consistent with the date of maturity and was tense and irritable. X-ray showed the spine to be flexed, but not crumpled. At 34 weeks, the patient spontaneously delivered a live premature infant showing unusual rigidity of the limbs. The head was molded obliquely. The mouth tended to remain open and contained a mildly adherent blood clot. There was no evidence of a bag of waters nor was there a gush of liquor during delivery. After respiration was established, the child progressed normally and is now 7 months old. The only remaining deformity was a talipes equinovarus of the right foot and a metatarsus varus of the left.

As far as can be determined, this is the only child developed extramembranously who has survived for so long a period. This must be partly due to the ante-natal care in helping the mother to carry the pregnancy to 34 weeks, and to delivery at 34 weeks before the contractures became too fixed.

degeneration of the epithelium and, frequently but not invariably, with the deposit of crystals of blood pigment, often in considerable amounts, in the tubules.

Almost concurrently the observations of Bratton (*Lancet*, 1941, 1: 345) and James Young (*Brit. M. J.*, 1942, 2: 715) showed that in certain types of obstetrical anuria, especially that seen in abruptio placentae, the kidney exhibits identical pathological changes. In abruptio, this lesion is limited almost conclusively to cases of concealed hemorrhage and in 20 abruptio cases of this type Young found it in 5, or in one-quarter. Since both in abruptio and in crush injuries there may be massive tissue damage to muscle, it seems conceivable that toxic metabolites of tissue origin may play an essential etiological role. The occurrence of this general picture, that is, anuria or oliguria in association with lower nephron degeneration, is less frequently seen in eclampsia; but practically all writers on the pathology of eclampsia have described, in a small percentage of cases, the presence of granular casts containing hemoglobin derivatives in the tubules of the medulla and in a few tubules of the cortex. J. F. Smith has examined necropsy material from 17 cases of eclampsia at the London Hospital and has found these pigment casts in the second convoluted tubules, the ascending limbs of Henle and in collecting tubules, in 3. In 2 of these 3 cases there was a clinical history of severe oliguria. Moreover, it has long been believed that abruptio is very closely allied to the toxemias; and, all in all, the evidence is suggestive that the anuria of certain cases of abruptio, of certain cases of eclampsia and of crush injuries may have a common denominator in lower nephron nephrosis.

More recently, experimental studies on the renal circulation under normal and abnormal conditions, carried out at the Nuffield Institute for Medical Research in Oxford, have thrown new light on the problem. These investigations have been summarized most lucidly in an important monograph, "Studies of the Renal Circulation," under the authorship of Josep Trueta, Alfred E. Barclay, Peter M. Daniel, Kenneth J. Franklin and Marjorie M. L. Prichard (Blackwell, Oxford, 1947). The gist of their findings is as follows. In the normal animal the vessels of the cortex receive the greater part of the renal blood supply, while those of the medulla receive a noticeably smaller part. Under certain experimental conditions, the reverse becomes true and the vessels of the medulla receive by far the greater part of the blood supply, while those of the cortex, with the exception of the vessels in its deepest zone, receive virtually none. When renal blood flow is diverted from the cortex to the medulla the pathway through which it is carried from the renal artery to the renal vein is through the vasa recta of the kidney. This mechanism by which the renal blood flow bypasses the cortex is known as the "Oxford shunt" or "Trueta shunt."

From an obstetrical point of view it is important to note that this short circuiting mechanism can be brought into operation by a neurovascular reflex. As an example of this type of action, stimulation of the central end of a divided sciatic nerve will produce it,—predominantly in the kidney located on the same side as the sciatic nerve stimulated. When, after such stimulation, methylene blue is injected into the left and right renal arteries in turn, the kidneys show a striking contrast in the distribution of the dye. Whereas the kidney on the stimulated side shows only a few isolated spots of blue on its surface, the kidney on the unstimulated side is irregularly stained with the dye over its entire surface. The most marked and constant examples of the shunt were obtained by faradic stimulation of the nervous plexus surrounding the renal artery. The authors were able to induce the shunt also by the injection of staphylococcus toxin and pituitary extract. In many of the experimental animals the shunt produced an almost complete ischemia of the renal cortex.

At a meeting of the Section of Obstetrics and Gynaecology of the Royal Society of Medicine on January 21, 1949, this whole renal problem in relation to obstetrical conditions was extensively discussed by obstetricians as well as physiologists and pathologists. From an obstetrical point of view an important point was brought out by Professor K. J. Franklin (one of the co-authors of the above monograph and a distinguished physiologist) in connection with what he calls "stretch stimuli." In experimental animals it was found that stretching the bladder by the introduction of saline solution at body temperature can reflexly evoke, to a varying degree, the renal shunt; the same was found true of isolated portions

OLIGURIA AND ANURIA IN TOXEMIA OF PREGNANCY

C. H. MAUZY AND J. F. DONNELLY

Bowman Gray School of Medicine, Winston-Salem, N. C.

Am. J. Obst. & Gynec., 57: 421-437, (Mar.) 1949.

Depression of renal secretion constitutes one of the gravest complications of pregnancy and recent obstetrical literature has failed to give this clinical picture its proper recognition. The incidence of urinary suppression associated with toxemia was 5 per cent in the authors' experience. The etiology of this symptom complex is obscure but it has been noted under numerous circumstances. A few of the apparent causes of oliguria or anuria are hemolytic transfusion reactions, nontraumatic muscular ischemia, uteroplacental damage, crush syndrome, toxemia of pregnancy, etc. The pathological picture is that of a lower nephron nephrosis. The kidneys are enlarged and pale and microscopically there is a varying degree of necrosis of the lower nephrons. The pathogenesis is not clearly understood but it is felt that there is release of nephrotoxic substances into the blood which cause tubular damage. In addition, there is liver damage with loss of detoxification properties. Injury to the lower nephron cells causes loss of selective resorption and hence there is urinary suppression.

The authors have presented 9 cases in which some degree of urinary depression developed during the time of toxemia of pregnancy. In this series there was only one death, though the course of several of the patients was quite stormy. Fluids were given in large amounts either before or during the period of anuria or oliguria in 7 of the cases and congestive failure developed in 3 of these cases. Premature separation of the placenta occurred in 3 cases. Only 2 cases resulted in a viable fetus and in these instances it was only because of prompt termination of pregnancy that a live baby was obtained.

In view of their experience, the authors feel that interruption of pregnancy is mandatory in such cases. In view of the tubular damage with leakage of the glomerular filtrate into the blood stream, excessive fluids will lead to cardiac decompensation and pulmonary edema; therefore, it is felt that the fluid intake should be restricted. Renal decapsulation is thought to be of questionable value, and peritoneal lavage is recommended for those patients who do not respond to ordinary methods of treatment. The plan of treatment which the authors feel is the most rational includes: (1) limitation of fluids; (2) maintenance of normal blood chemistries; (3) ureteral irrigation; (4) renal decapsulation; (5) peritoneal irrigation; and (6) supportive measures.

(This paper touches upon a renal problem which is receiving intensive study in England and about which obstetricians in this country may be hearing more and more as time goes on. It had its genesis, if I am not mistaken, during the war when it was observed that persons suffering from crush injuries often developed fatal anuria. A characteristic lower nephron lesion was described in these cases by Bywaters and Dible in 1942 (J. Path. & Bact., 1942, 54: 111). It affected the second convoluted and collecting tubules and was associated with

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MAURICE J. DRELL

Seattle, Washington

West. J. Surg., Obst., & Gyn., 56: 455, 1948.

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Pregnancy has been mentioned as an etiologic factor in subconjunctival ecchymosis, transitory paralysis of accommodation, optic neuritis and bitemporal hemianopia. Many of the hemianopic changes are undoubtedly functional but, in some instances, mild changes of short duration probably take place.

In a group of 200 cases reviewed by Hallum (*Arch. Ophth.* 37: 472, 1947), in those patients considered as having severe toxemias, positive ophthalmoscopic findings were present in 98%, albuminuria was present in only 68%, casts in 26%, azotemia in 5%, a lowered phenolsulfonphthalein test in 45%, and excessive weight gain in 7.5%.

Whatever the origin of toxemia, the changes in the fundus are those of vascular spasm and its consequences. The essential feature in vascular spastic disease is narrowing of the arteries. Concomitant with the spastic narrowing of the lumen, the light streak reflected from its blood column becomes narrowed. As the process develops, the retina becomes edematous, the area loses its normal orange-pinkness, and the permeability of the vessel walls is impaired, permitting the diapedesis of blood cells or serum. In extreme cases, the retina becomes lifted off from the underlying tissues by a layer of sub-retinal edema fluid to form a simple detachment. Visual loss follows, but the retina almost always reattaches itself in 10 to 14 days.

The stages outlined above are vasospastic in origin and are designated as purely hypertensive. They are associated with mild degrees of toxemia; these patients can continue to be treated conservatively. Perineural edema and focal or generalized constriction of the arterioles, plus hemorrhages or exudates or both indicate a severe breach in the vascular integrity. These fundus changes are an adequate indication for termination of the pregnancy. In patients who have had eclamptic convulsions, retinal detachment or papilledema or massive hemorrhage is observed in addition to the above changes. A very accurate prognosis may be made by observing the fundi.

Two other vascular complications of the eyes occur in pregnancy, but are not related to any generalized vascular diseases: occlusion of the central retinal

of the intestine and the nonpregnant and pregnant uterus. In other words, the renal cortical blood flow can be diverted in whole or in part through the incomplete adaptation of these hollow viscera to such changes of content as the investigators, in their acute experiments, attempted to impose. As an especially striking example of the stretch stimulus as applied to the pregnant uterus, Professor Franklin refers to an experiment carried out by one of his associates, Professor Amoroso. In the rabbit, the several conceptuses are spaced out in the uterus, and in consequence there is room for each, as it grows to encroach on the intervening "no man's land." Professor Amoroso ligated the uterus on each side of each conceptus early in gestation and so caused a more natural stretch, as the conceptus grew, of the uterine muscle enclosing them. This put the shunt mechanism on such a hair trigger basis that mere laparotomy and a touch to a conceptus region caused immediate diversion of the renal cortical blood flow. Professor Franklin advanced the hypothesis that toxemia of pregnancy is, or includes, a progressively increasing tendency for the renal shunt to be brought into operation, and that fatal bilateral cortical necrosis is the maximal irreversible result of this tendency.

Mr. T. L. T. Lewis described the clinical and pathological pictures presented by fatal cases of anuria in which a diagnosis of symmetrical cortical necrosis of the kidney is made postmortem and fatal cases of anuria in which a diagnosis of lower nephron nephrosis is made. In 1941 Duff and More of Montreal analyzed 71 reported cases of cortical necrosis of which 48 had occurred in pregnancy. Of these 48 cases two-thirds were in patients over the age of 30, 50 per cent had been preceded by abruptio and 25 per cent by eclampsia. The condition is characterized clinically by extreme oliguria with hematuria. On the basis of experiments by De Navasquez and other evidence, Mr. Lewis notes that even in the earliest stages of development of necrosis of the renal cortex, it is tremendously engorged with blood and the eventual ischemic necrosis is brought about by a failure of blood to circulate through a cortex stuffed with red blood cells. In lower nephron nephrosis the pathological features are strikingly different from those of cortical necrosis inasmuch as the renal cortex is extremely ischemic and the medulla is engorged; the glomeruli are living and have a healthy appearance and the characteristic lesion is in the second convoluted and collecting tubules; and there the epithelium shows various stages of damage, necrosis and desquamation and the lumina contain pigmented ribbon casts while sometimes the blood vessels near the tubules appear to have ruptured into them. Mr. Lewis then raises the question as to the possible connection, if any, between these 2 different pathological conditions. All the evidence, he believes, points to there being a circulating toxin involved, always in cortical necrosis, often in lower nephron nephrosis. It is conceivable in his opinion that, following a sudden release of toxic products into the circulation as, for example, following the absorption of uterine muscle breakdown substances in concealed abruptio hemorrhage, the kidney deals with the toxin presented to it in one of 2 ways: either a protective mechanism is brought into effect, and by means of a remote neurovascular or local toxin induced mechanism, the blood with its toxin is shunted from the cortex to the medulla so as to save the cortex from the action of this toxin; or else this protective mechanism fails and the specially susceptible cortical vessels become injured by the toxin, paralyzed, engorged and finally blocked. In the first case, lower nephron nephrosis results and in the second cortical necrosis.

The observations described above stand in the forefront of the attack which is being made today on the physiology and pathology of the kidney, especially in relation to the causation of anuria. These studies represent work in progress and there are obviously many loose ends still to be tied up. Nevertheless, the explanation of the anuria in such cases as those presented by Mauzy and Donnelly is probably to be found in certain of the concepts reviewed; and very possibly the altered water metabolism of pre-eclampsia and eclampsia may eventually find elucidation in some of these newly discovered renal mechanisms.—Ed.)

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Two other vascular complications of the eyes occur in pregnancy, but are not related to any generalized vascular diseases: occlusion of the central retinal

artery and thrombosis of the central retinal vein. In occlusion of the central retinal artery, the arteries are collapsed, with small clumps of red cells passing slowly through them. Intravenous papaverine and paracentesis of the anterior chamber must be administered immediately to be effective.

Ocular complications in the fetus include interstitial keratitis, ophthalmia neonatorum, multiple congenital defects, retrolental fibroplasia, and an encephalomyelitis caused by toxoplasma.

(This is a valuable summary of the ocular conditions most commonly encountered in obstetrics. Retinal examination is not only of value in demonstrating the severity of a toxemic process, but also in distinguishing acute toxemia (pre-eclampsia and eclampsia) from chronic hypertensive vascular disease. In the former, vasospasm and edema are the characteristic changes; whereas, in the latter, the pathognomonic alterations are arteriovenous compression, unsymmetrical arteriole constrictions, increased light reflex and, in severe cases, hemorrhages and exudates. It has been my experience that hemorrhages and exudates usually indicate pre-eclampsia superimposed on chronic vascular disease. I have rarely seen them in pre-eclampsia alone or in eclampsia alone. The acute nature of the process which causes the hemorrhages and exudates in these cases, and the chronic nature of the process responsible for the arteriovenous compression, light streak, etc., are shown by the fact that, within a few weeks after delivery, the hemorrhages and exudates disappear while the vessel changes persist indefinitely.)

The author is fully justified in stressing the fact that hemorrhages and exudates call for immediate termination of pregnancy. However, it must be remembered that these findings are rarely encountered except in very sick women and that astute judgment must be exercised in choosing a method for terminating pregnancy which carries with it the least possible trauma. Very often simple rupture of the membranes is the procedure of choice.—Ed.)

EFFECT OF THE LOW SODIUM DIET AND THE RICE DIET ON ARTERIAL BLOOD PRESSURE

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Am. J. Med., 5: 815, 1948.

Nine patients with essential hypertension were treated by diet; 7 received a low sodium diet adequate in protein; 4 received the rice diet in addition; one had the rice diet alone. Each patient was studied in a control period of one month prior to the institution of dietary therapy. The low sodium diet provided 1,800 calories, 70 gms. of protein and 300 mg. of sodium. The rice diet contained 2,000 calories, 20 gms. of protein and 150 mg. of sodium. Blood pressure, urinary output, and blood and urinary sodium were recorded.

In all patients, the urinary sodium excretion fell, but the levels on the rice diet were somewhat lower than on the low sodium diet. Weight loss ranged from $4\frac{1}{2}$ to 14 pounds. In 4 patients on low sodium diet there was a fall in blood pres-

sure; in 3 there was no change. In 3 of the patients on the rice diet, there was a fall in blood pressure. The effect of the rice diet was only slightly greater than that of the low sodium diet in producing a fall in blood pressure. In the series there was only one patient whose blood pressure fell to normal values.

In the patients with a fall in blood pressure after dietary therapy, there was no relief of symptoms. The authors conclude that dietary therapy is of little value in the management of essential hypertension.

(Obstetricians are naturally interested in the widespread attention which internists are giving to salt restriction in essential hypertension because of its possible bearing on the toxemias of pregnancy. The results have been somewhat contradictory and the above authors plainly find it of little value. However, the management of pre-eclampsia, especially in the presence of edema, is a different problem and here there is general agreement that salt restriction is a most important part of the treatment, perhaps the most important. With the availability of salt-free milk, salt-free bread and other salt-free foods, this regime is being pushed by some obstetricians to levels of sodium intake which approximate 0.5 Gm. per day. The usual "salt-poor" diet provided in most hospitals contains about 4 Gm. of sodium chloride, or approximately 1.6 Gm. of sodium.

That special foods have to be utilized to bring the sodium content of the diet to 0.5 Gm., is shown by the fact that a quart of milk contains 0.5 Gm. of sodium while an ordinary slice of white bread contains about 0.2 Gm. Moreover, in some localities, the water used for drinking contains significant amounts of sodium and, unless analysis shows that it contains less than 3 mg. per liter, it is necessary to substitute distilled water. In a few localities the public water supply contains 5 times this quantity of sodium; and if a 2 liter intake be assumed, this would mean 0.3 Gm. of sodium just from water. The sodium in milk can be almost completely eliminated by the use of a low sodium milk powder, such as Lonalac which was especially designed to provide a protein food of animal origin suitable for liberal use in low sodium diets. Salt-free bread can also be secured prepared with Lonalac. Salt "substitutes," designed to give foods a salty taste, had best be avoided until their safety can be proved. As most will recall from newspaper notices, several serious cases of poisoning recently resulted from the use of such a preparation containing lithium chloride.

In a very limited experience, extreme salt restriction has not proved especially gratifying in my own hands. Patients complain about it and the results have not impressed me as being better than with the usual "salt-poor" diets provided by most dietary departments. However, I may well be wrong about this.—Ed.)

AN EFFECT OF PYRIDOXINE ON BLOOD UREA IN HUMAN SUBJECTS

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J. Biol. Chem., 178: 511, 1949.

In 1942 pyridoxine was related to protein metabolism. The drug has been used with apparent success in the alleviation of nausea and vomiting in pregnancy and also of the same condition consequent to irradiation. This report deals

with the response obtained in blood urea levels before and after administration of pyridoxine in cases of nausea and vomiting in pregnancy.

Three groups of subjects were used: (1) non-pregnant females on a constant protein intake for 5 days before blood samples were taken, (2) pregnant females with no apparent abnormality, (3) pregnant patients classified clinically as showing hyperemesis gravidarum. In all cases, identical dosage of pyridoxine was employed—oral administration of 40 mg. of pyridoxine hydrochloride in 3 successive days. The effect of a test load of DL-alanine on the blood urea was determined.

The fasting blood urea was less in normal pregnant than in non-pregnant women. In cases of hyperemesis gravidarum, the blood urea was decreased below the value normally characteristic of pregnancy. Blood urea was increased after the administration of pyridoxine only in subjects suffering from nausea and vomiting. Blood urea is decreased during pregnancy; it may be apparent as early as the 6th week of gestation. Within a few days after delivery, blood urea rises to the normal non-pregnant level. Changes in blood urea after a test load of alanine were similar in normal pregnancy to those observed in non-pregnant persons. Subjects with hyperemesis gravidarum showed an abnormal response which was corrected after pyridoxine administration. The normal sequence after the test load is a maximum value for blood urea at the 6th hour and a decrease to the original level by the 12th hour; the abnormal response is a failure of the blood urea to decrease between the 6th and 12th hours.

The results reported may be interpreted as presumptive evidence that in cases of nausea and vomiting, pyridoxine insufficiency was exhibited. It might be assumed that the failure of pyridoxine to produce any effect in non-pregnant and normal pregnant subjects was due to the absence of a deficiency of the vitamin.

(This study represents an attempt to demonstrate that pyridoxine deficiency does exist in hyperemesis gravidarum and the evidence which the authors advance is rather convincing. As is true of other agents which have been recommended for this condition, pyridoxine is sometimes successful and sometimes not, but there is substantial evidence that deficiency of the B complex in general plays an important role in many of these cases. Theoretically, the evidence that thiamine deficiency may cause nausea and vomiting is especially strong in view of the several studies showing that gastro-intestinal motility is regularly inhibited when the intake of this vitamin is inadequate; thiamine deficiency also inhibits the normal secretory functions of the stomach and probably of the intestinal tract. (Sollman: A Manual of Pharmacology, 7th Edit. Saunders, 1948, P. 89.)

Fortunately, hyperemesis is less a problem to-day than it used to be. Thus, in 35,000 obstetrical admissions to our service in the last two decades, only one therapeutic abortion was performed for this complication; whereas in 33,000 admissions prior to 1930, interruption of the pregnancy was deemed necessary in 20 cases. The regular inclusion of liberal amounts of the B complex in the therapy of hyperemesis has doubtless contributed, along with other factors, to this change.—Ed.)

DANGER OF DICUMAROL TREATMENT IN PREGNANCY

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J. A. M. A., 139: 758-762, 1949.

The increasing use of dicumarol in the prevention and treatment of thrombo-embolic phenomena brings up the clinically significant question whether this drug, when given to a pregnant woman, has deleterious effects on the growth and development of the fetus. Previous reports on experimental observations in animals would tend to indicate that dicumarol is quite toxic to the fetus. In the present study, the rabbit was selected because of its short gestation period. Sufficient dicumarol was given to elevate the prothrombin to levels within the so-called "safe" range. The lower limit of the safe range was arbitrarily set at 10 per cent of normal, as is commonly done in the dicumarol therapy of humans.

The effect of continuous dicumarol administration on the intrauterine growth and development of the fetus of the pregnant rabbit was then observed. When dicumarol was given in doses which produced an unsafe level of prothrombin (below 10 per cent of normal) in the mother, even for not more than 2 days, the fetuses died in utero. They were small, showing conspicuous maceration of the skin and decomposition of the organ tissues. When "safe" prothrombin levels were maintained in the mother, the infant rabbits revealed an extreme decrease in their prothrombin at birth, with a definite hemorrhagic tendency. However, the mothers did not experience excessive intrapartum or postpartum hemorrhage.

Dicumarol affects the prothrombin level of infants to a much greater extent than that of the mother. Although animal experiments may not be directly applicable to human beings, it would appear that dicumarol treatment is not advisable in the pregnant woman, since it may seriously interfere with the normal development of the fetus or cause fetal death.

(These observations confirm the earlier work of Quick and can leave little doubt that, in the rabbit at least, dicumarol exerts a most deleterious effect on the fetus. As the authors point out, it does not necessarily follow that similar effects would accrue in human pregnancy. Nevertheless, in view of the experimental evidence, it would seem exceedingly hazardous to try dicumarol in a pregnant woman unless extensive evidence to the contrary can be adduced.—Ed.)

URINARY TRACT INFECTIONS DURING PREGNANCY

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N. Orleans M. & S. J., 101: 490, 1949.

The incidence of urinary tract infections in the female is greater during pregnancy. Pyelonephritis occurs in about 2% of all pregnant patients. Cortical abscesses are unusual; bacteremia is seldom found. Hydroureter and hydronephrosis are physiologic during pregnancy; should this physiologic stasis be associated with infection, the amount of stasis tends to increase. When chronic pyelonephritis persists over a long period of time, it has been shown that hypertension may result.

Urinary tract disease during pregnancy may cause low grade infections without symptoms. Pain is the most frequent symptom. When frequency of urination is accompanied by dysuria or strangury, an inflammatory process is suspected. The clinical manifestations of the disease appear most commonly during the 2nd and 3rd trimesters. The most important procedure in diagnosis is proper urinalysis; a catheterized specimen should be used. Test of kidney function is essential in determining the extent of the infection. Cystoscopy and radiography are essential for complete diagnosis.

The majority of patients do not require hospitalization and can be treated with sulfadiazine, 0.5 to 1 gram after meals and at bedtime. In severe infections, bed rest, analgesics, a high fluid intake and sulfadiazine and penicillin are advised. Most of the patients with severe urinary tract infection during pregnancy should be given blood. If prompt response does not occur, the patient is considered a candidate for cystoscopy and indwelling ureteral catheters. In severe infections due to *Escherichia coli*, *Proteus vulgaris*, *Aerobacter aerogenes*, *Pseudomonas aeruginosa*, *Hemophilus influenzae*, and *Mycobacterium tuberculosis*, streptomycin is the antibiotic of choice. With the exception of tuberculosis, there should be response in 48 to 78 hours.

Due to the antibacterial agents, patients now rarely require termination of pregnancy for the control of urinary tract disease. In toxemia of pregnancy and sickle cell anemia in the Negro, interruption of pregnancy is necessary to abort the progression of the disease.

The prognosis for the mother and infant is excellent. In future pregnancies, there is likely to be a recurrence of the urinary tract disease. The authors have not noticed congenital malformations of the offspring of patients with severe pyelonephritis.

SEVERE HYPERLIPEMIA ASSOCIATED WITH
NONDIABETIC PREGNANCY
REPORT OF A CASE

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Arch. Int. M., 82: 339, 1948.

The authors report the only case in which lipemia retinalis is reported complicating a pregnancy in a nondiabetic patient. It is the second case in which autopsy was performed while the disease was active. The milky blood serum and the unusual appearance of the retinal vessels form a striking picture which cannot be missed. It is noted by a survey of the literature that lipemia retinalis usually accompanies acidosis, either of diabetes or of other toxic states.

The patient was a 19 year old woman admitted in the 8th month of pregnancy. She was asymptomatic and milky blood serum was discovered on routine serological examination. On physical examination the retinal arteries were cream-colored and were surrounded by a very pale retina. The veins were chocolate in color; there were no hemorrhages or exudates. The blood counts were not unusual for this stage of pregnancy. Urinalysis was negative. The fasting blood sugar was 67 mg.%, cholesterol 248 mg.%, carbon dioxide combining power 82%. Glucose tolerance test was not unusual. The total serum lipids were 8,288 mg., fatty acid 7,685 mg., phospholipids 7.5 mg., cholesterol 760 mg., and cholesterol esters 430 mg., upon recheck of the blood by the New York Postgraduate Medical School. Numerous fat vacuoles were seen in the red and white blood cells. The patient remained asymptomatic and it was felt that she should be allowed to go to term. She went into labor spontaneously, but after 15 hours of labor she complained of excruciating abdominal pain, went into shock and the fetal heart disappeared. The patient was treated with plasma and a surgical consultation was obtained. The diagnoses of intraperitoneal hemorrhage, acute pancreatitis, lipid coronary insufficiency, lipid pulmonary emboli, and multiple renal or mesenteric emboli were considered. At laparotomy, 750 cc. of milky fluid was obtained from the abdomen. The pancreas appeared normal. It was felt that no further surgery was necessary. Postoperatively 5 liters of whole blood were required. Ten hours postoperatively the patient was delivered of a stillborn term infant who showed no gross abnormalities. Eighteen hours postoperatively the patient died. Terminally she showed abdominal fluid and failure of the peripheral circulation.

At autopsy, the retroperitoneal area was filled with blood clot which dissected into the mesocolon. The liver was not enlarged. There was a 3 cm. area of thrombosis at the entry of the splenic vein into the portal vein. The pancreas was moderately enlarged. Microscopically, the liver showed minimal fatty infiltration. The pancreas showed extensive diffuse necrosis with heavy fibrosis. The normal

splenic architecture was replaced by a diffuse pattern of round cells with centrally placed nuclei. The remainder of the autopsy was non-contributory.

It is possible that the fibrosing pancreatitis which was present resulted in a deficiency of lipase with resulting hyperlipemia. The increased metabolism of fat which occurs in pregnancy might thus have been aggravated. It was suspected that the uterine contractions might have propagated a fat embolism which initiated the portal vein thrombosis. In retrospect, the authors wonder whether early cesarean section prior to the fatal acute episode might have given a better outcome.

SPONTANEOUS RUPTURE OF THE UTERUS IN LATE PREGNANCY ACCOMPANIED BY PLACENTA ACCRETA

M. H. MEYERHARDT

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J. Missouri M. A., 46: 177-180, (Mar.) 1949.

Placenta accreta is a rare condition, the incidence varying from one in 6000 to one in 50,000 cases in the large obstetrical clinics. The etiology is unknown but many factors have been suggested as playing a role. The manual removal of the placenta in previous labors with damage to the muscular layers of the uterus may be one such factor. Atrophy and scar tissue formation following the use of radium or subsequent to the so-called war amenorrhea has been suggested in an etiologic role. Submucous myomata with accompanying coincident atrophy of the endometrium above the tumor and diverticulum of the uterus have been mentioned. Scars of previous classical cesarean sections and perforations of the uterus also offer good grounds for the development of placenta accreta.

The writer has summarized 3 cases found in the literature of placenta accreta which was associated with rupture of the uterus in late pregnancy. He has added a case from his own experience which showed this same combination. His case was that of a 23-year-old white female, gravida 3, para 1, who was admitted to the hospital at term with mild abdominal cramps. With her first pregnancy she had had retained placenta, and a dilatation and curettage was done 3 weeks after delivery. The second pregnancy was terminated by an abortion and curettage was again necessary. In the pregnancy reported, the patient had experienced a sudden tearing sensation in the abdomen and this was immediately followed by painful contractions. After 3½ hours of such pains the head was easily palpable in the fundus and the presenting part disappeared from the pelvis and was replaced by a peculiar bulging in the cul-de-sac. The patient went into shock, so that rupture of the uterus was suspected and immediate laparotomy was performed. On opening the abdomen, a large amount of blood and fluid was found

and a dead fetus was lying free in the peritoneal cavity. The uterus appeared to have completely everted itself and the placenta was attached to the posterior portion of the fundus. A supravaginal hysterectomy was done and the patient made an uneventful recovery.

Microscopic examination of the uterus and placenta showed deep penetration of the trophoblast into the uterine musculature. The uterus also showed a marked degree of diffuse adenomyosis. This case shows such penetration of villi that there can be no doubt of the cause of the spontaneous rupture. 7 figures.

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PATHOLOGY OF LABOR AND PUERPERIUM

THE MANAGEMENT OF THE PROBLEMS ASSOCIATED WITH PROLONGED LABOR

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N. Y. State J. M., 48: 2601, 1948.

Patients who experience prolonged labor are subject to all the hazards associated with difficult labor and delivery. The uncertainty regarding the ability of the uterus to perform in a normal manner during parturition makes every parturient a possible candidate for labor dystocia.

Labors exceeding 20-24 hours in length are defined as prolonged. Labor is not said to have been established until the uterine contractions produce definite changes in the cervix.

The etiology of prolonged labor may include (1) abnormal development of the uterus, (2) overdistention of the uterus, (3) rapidly succeeding pregnancies, (4) multiple myomata and (5) miscellaneous factors. Hormonal imbalance and derangement of calcium or potassium metabolism may also play a role in the etiology of prolonged labor. The tocographic studies of Murphy have shown that prolonged labor is associated with poor uterine contractility. Failure of the cervix to dilate may be associated with the presence of an excessive proportion of fibrous tissue. The cervix may act as a sphincter and fail to dilate.

The maternal risk is not greatly increased during prolonged labor if rest and fluid balance are properly maintained. Fetal mortality is markedly increased. The major cause of fetal death is intrauterine asphyxia. Intracranial hemorrhage resulting from traumatic vaginal delivery has decreased in frequency.

In the best interest of the infant, 30 to 40 hours of labor is the maximum time permissible for labor. Posterior pituitary extract intramuscularly in $\frac{1}{2}$ -1 minim doses may be used in the presence of desultory labor if cephalopelvic disproportion is not present. Tetanic contractions are rare and almost always result from the first dosage rather than subsequent ones. Pituitary extract should produce complete cervical dilatation in 3-4 hours. If this is not the case, further therapy may produce intrauterine asphyxia and is likely to be of no value. Delivery should be accomplished in the least traumatic manner. If the cervix is more than half dilated, the presenting part near the pelvic floor, and the outlet ample, pelvic delivery should be performed using Dührssen's incisions if necessary. If these conditions are not present, cesarean section is probably safer. In general, an extraperitoneal section is indicated. Generous use of antibiotics is also advisable.

THE ASSIMILATION PELVIS AS AN
OBSTETRICAL PROBLEM

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Ztschr. f. Geburtsh. u. Gynäk. 129: 174, 1948

The assimilation pelvis is defined as one in which the pelvis is either lengthened or shortened by the inclusion of the last lumbar vertebra in the sacrum or the lumbarization of the first sacral vertebra. All types of union between the last lumbar and the first sacral vertebrae are reported, from complete bony union to unilateral bony union. Pelves which contain more than the usual 5 sacral vertebrae are designated as high assimilation pelves.

Kirchhoff designates 3 types of assimilation pelves. 1. Transitional pelves. The general form of the pelvis remains normal but an anatomically or functionally fully assimilated last lumbar vertebra lengthens the pelvis and produces a double sacral promontory. 2. Assimilation pelvis with 6 sacral vertebrae but retention of normal dimensions. An anatomically and functionally fully assimilated vertebra lengthens the pelvis by the height of one vertebral body but it has entirely accommodated itself to the sacrum so that the pelvic dimensions are within normal limits. 3. Assimilation canal pelvis. The pelvis is not only lengthened but is lacking in depth so that it is of unsatisfactory dimensions throughout. This third group is the most common.

If the sacral promontory is excessively high the angle made between the true conjugate and the ventral surface of the sacrum becomes more acute. On the average this angle is 110 degrees. If the angle is under 80 degrees the number of complications rapidly increases. If the promontory be unusually high, the vertex will be driven forward toward the symphysis and will tend to rotate into an occiput posterior position. Moreover, if a double sacral promontory exists there may be a point below the level of the true conjugate where the anterior-posterior diameter is less than the latter. Consequently dystocia may result at this "narrowest point." Finally, in the assimilation canal pelvis the vertex, if it should be able to pass the inlet, characteristically is arrested in midpelvis. This is because of the lack of adequate midpelvic dimensions.

In a series of 212 cases of high assimilation pelvis, Kirchhoff reports the following statistics: spontaneous delivery 109, 51.5 per cent; cesarean section 47, 22.2 per cent; forceps, 39, 18.4 per cent; perforation 9, 4.2 per cent; version 8, 3.7 per cent; deflection attitudes 9, 4.2 per cent; breech presentation 13, 6.2 per cent; high arrest 4, 1.9 per cent; maternal deaths 4, 1.9 per cent; fetal deaths 15, 7.1 per cent; and average duration of labor 24 hours.

(The very high incidence of operative interference in this series of high assimilation pelves is surprising. Assimilation is an extremely common pelvic anomaly, being demon-

strable in at least a quarter of all women. Thus, McLane demonstrated it by x-ray in 24.4 per cent of 164 patients at the New York Lying-In Hospital and other authors have reported even higher figures. We have also noted it frequently in the course of x-ray pelvimetry but have not observed that it is an important cause of dystocia. Kirchhoff's opinion, moreover, does not seem to be shared by other German authors. Thus, L. Seitz, in Stoeckel's "Lehrbuch der Geburtshilfe" (5th Edit. 1938), writes as follows about the clinical aspects of assimilation pelvis: "Viewed from an obstetrical viewpoint, the derangements are usually so slight that they do not interfere with the mechanism of labor appreciably." These pelvises, however, do tend somewhat to resemble a male pelvis and moderate degrees of mid and outlet pelvic contraction are occasionally observed.—Ed.)

THE NEWBORN

ANTEPARTUM DIAGNOSIS OF CONGENITAL HEART DISEASE

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Ztschr. f. Geburtsh. u. Gynäk. 129: 55, 1948

The author reports 2 cases of congenital heart disease in which the diagnosis was made antepartum. In the first case the fetal heart was auscultated at a rate of 80 prior to the onset of labor and it remained at this rate throughout labor without being influenced by contractions. Accordingly, congenital heart disease was suspected. Because this diagnosis was entertained, operative delivery was not performed, although interference might have been proper if the slow fetal heart rate had been interpreted as due to fetal distress. The infant was a full term male who was normal in all respects, both on physical and roentgenological examination. Electrocardiographic studies, however, revealed complete heart block. The auricular rate was 120 and there was an idioventricular rhythm of 92, with polytopic individually interpolated and retrograde extrasystoles.

In the second case coupling of the fetal heart sounds was observed every 10-13 beats, as well as an extrasystole every 3 beats. This irregularity persisted throughout labor without regard to the status of the mother or the state of contraction of the uterus. Prolapse of the cord did not occur, and when the placenta was delivered there were no anomalies therein. Electrocardiographic studies of this infant postpartum showed very frequent ventricular extrasystoles. The same electrocardiographic picture was present 1 week later.

The etiology of the second case is not yet clear. In the first case it was believed that a septal defect resulted in failure of auriculoventricular conduction. With respect to the second case it may be said that the prognosis of the majority of idiopathic intrauterine arrhythmias is good.

The author concludes that the fetal heart tones must be carefully observed, not only with regard to their presence or absence, but also with regard to their strength and their rhythmicity. As demonstrated in these cases, it is perfectly possible to diagnose or at least strongly to suspect the presence of congenital cardiac disease prior to delivery. Such a diagnosis may have an important influence upon the management of the labor.

(In 1934 Dippel reported 2 cases of congenital heart disease from our clinic in which the diagnosis was made before birth (*Am. J. Obst. & Gynec.* 1934, 27: 120). Since then several other similar cases have been recorded.

In Dippel's first case the fetal heart presented a peculiar blowing sound which was at first thought to be a funic souffle. Further auscultation, however, revealed a definite irregularity. Moreover, deep pressure with the stethoscope failed to affect either the intensity

or duration of the murmur; and a diagnosis was made of a structural anomaly of the fetal heart. After birth a long, loud systolic murmur was present. The infant did poorly and died 60 hours after delivery. Autopsy showed extensive cardiac malformations, including transposition of the great vessels, a very large patent foramen ovale, a rudimentary tricuspid valve, a rudimentary left ventricle, a markedly hypertrophied and dilated right ventricle, a small patent interventricular septum and small hemangiomas on the leaflets of the mitral valve. This case has been reviewed because it shows how an astute examiner can occasionally make the diagnosis of fetal heart disease before birth largely on the basis of adventitious sounds.

In Dippel's second case the fetal heart was only 50 per minute and this rate persisted throughout labor. This baby also died several days after birth and autopsy showed a stenosis of the arch of the aorta, patent foramen ovale, defect in the interventricular septum, patent ductus arteriosus and extensive central liver necrosis with chronic passive congestion of the liver and hemorrhages in the lungs.

Dippel points out that investigators have concerned themselves chiefly with the rate of the fetal heart and that only a few have studied the character of the sounds themselves. The great majority of cases reported have been instances of true sinus arrhythmia. These are not infrequently encountered in the prenatal course and are characterized by the fact that they disappear either immediately or within 10 to 15 days after delivery. Such sinus arrhythmias are of little or no clinical significance and are probably best explained on the basis of a myogenic or neurogenic origin, the young heart having a relatively unstable pacemaker. It is very probable that Weidenbusch's second case belongs in this category. The literature up to 1934 is reviewed in Dippel's paper.—Ed.)

REPRODUCTIVE HISTORIES OF THE MOTHERS OF 322 INFANTS WITH ERYTHROBLASTOSIS

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Pediat., 2: 369-381, October, 1948

The author finds that in evaluating any method of treatment of erythroblastosis, the previous reproductive histories of the mothers of the treated infants must be taken into account. In her hands, the previous maternal history has been of more value in prognosticating the fate of an infant born to an immunized Rh-negative woman than have changes in maternal antibody titer or differences in the variety of antibodies present.

Reproductive histories have been obtained from 175 Rh-negative women, observed since 1934, who had a total of 699 pregnancies prior to January 1, 1948. These included 341 fetuses and infants delivered before the birth of the first erythroblastotic infant, 179 born in pregnancies producing the first erythroblastotic infants, and 179 born in subsequent pregnancies.

Only 7 women gave no history of a pregnancy prior to the birth of an erythroblastotic infant and 4 of these had received multiple transfusions before becoming

pregnant. Thus, in 98.3 per cent of the total number of women, a pregnancy or transfusion was the possible cause of immunization.

Of the 341 pregnancies preceding the birth of the first infant with erythroblastosis, there resulted 7 stillbirths, 13 neonatal deaths, 65 abortions and 256 surviving children. Forty-four of these abortions followed the birth of the last normal child and preceded the birth of the first erythroblastotic child. The number of unsuccessful pregnancies in the total group of 175 women is abnormally high. Only 75 per cent of the recorded pregnancies ended successfully; 19 per cent ended in abortion and 6 per cent in stillbirth or neonatal death. These figures were compared with the reproductive histories of 2410 consecutively discharged patients in 1947, each of whom had had fewer than 6 pregnancies and none of whom gave birth to an erythroblastotic infant. Two thousand and fifty-three (85.2 per cent) of this control group were Rh-positive and 357 (14.8 per cent) were Rh-negative. Fewer than 11 per cent of the pregnancies in the control groups were unsuccessful, while 24 per cent of the pre-erythroblastotic group ended in abortion, stillbirth or death. The latter group averaged only 1.4 living children in comparison to 1.7 for the control groups. In the 2 control groups, 85 per cent of the Rh-positive women and 84 per cent of the Rh-negative women had had no unsuccessful pregnancies, while in the pre-erythroblastotic group only 62 per cent had had no unsuccessful pregnancies.

The diagnosis of erythroblastosis was made for the first time in 7 women in a first pregnancy and in 168 women in second or subsequent pregnancies. Of the 178 infants delivered as the first child known to have erythroblastosis, 56 died before birth, 60 died after birth and 62 survived. Seventy-five per cent of all women giving birth to erythroblastotic infants delivered their first affected child before the fourth pregnancy. The place in the family of the first affected child is slightly earlier among those who survived than among those who died or were stillborn. In this group, only 7.5 per cent of all infants who were born alive died if they survived the third day.

Ninety-six women had 179 pregnancies following the birth of an infant with erythroblastosis. These have ended in the birth of 3 Rh-negative, 144 Rh-positive infants with erythroblastosis and 32 abortions. Thirteen of the abortions are known to have been induced. Of the Rh-positive infants, 69 were stillborn, 63 died and only 12 survived. Three of the latter are known to have brain damage.

Thus, a total of 322 erythroblastotic infants and fetuses were delivered. Of these, 74 lived, 123 died and 125 were stillborn. Of the infants who lived, all but 12 (16 per cent) were the first affected children to be delivered. Of the infants who died, 132 (53 per cent) were delivered following the birth of an erythroblastotic infant.

The 322 infants with erythroblastosis included 158 males, 132 females and 32 of unknown sex. Twenty-eight per cent of affected males and 23 per cent of affected females survived.

Among 131 erythroblastotic infants delivered in the Chicago Lying-In Hospital the mortality rates were: 38 per cent for 58 infants whose birth had not been immediately preceded by a transfusion, abortion or erythroblastosis in a sibling; 74 per cent for 27 infants whose birth was immediately preceded by an abortion

or transfusion; and 90 per cent for 46 infants whose birth was preceded by that of an infant with erythroblastosis.

Among 18,468 deliveries at the Chicago Lying-In Hospital in the last 5 years, the frequency with which erythroblastosis occurred for the first time varied from once in 2,814 deliveries for women in their first pregnancies, to 1:172 in second pregnancies, and to 1:55 for sixth pregnancies.

In 1946 and 1947, 44 erythroblastotic infants and fetuses were delivered at this hospital. *In no instance did a live born infant die whose birth had not been preceded by that of an infant with erythroblastosis. In only 2 instances did an infant survive whose birth had been preceded by that of an infant with this disease.*

(The two concluding, italicized sentences of this abstract will prove comforting to obstetricians who have been perplexed and sometimes actually misled by the behavior of maternal antibody titer as pregnancy advances. These sentences emphasize the importance of past history which, in Dr. Potter's opinion, is of greater prognostic import than change in antibody titer. There can be no doubt that bizarre immunological circumstances may occasionally invalidate entirely any deductions to be drawn from antibody titer. Thus, I recall a case in which the titer was high throughout pregnancy and in the last trimester zoomed to astronomical figures. The baby was relegated in our minds to inevitable doom (as it was also by the husband who was so informed); but at delivery and afterwards it was apparent that a finer infant never was born. A searching re-evaluation of the bloods of mother, husband and infant by expert immunologists showed that we were dealing with an extraordinarily rare and intricate combination of atypical antigens and antibodies and that the whole series of events, on retrospect, was entirely understandable. Cases like this are unusual but they happen often enough so that obstetricians are becoming wary about positive antibody reports and do not give them as much weight as they did several years ago.

On the other hand, it is possible to over-emphasize and over-simplify the significance of past history. This also has its pitfalls and blind alleys. It is true that if a woman has had a previous erythroblastotic child and if her husband is homozygous, the outlook is grave. However, there is about an even chance that the husband is heterozygous (which can usually be proved); and if so, there is another 50-50 chance that the baby will be Rh negative and hence unaffected. Accordingly, if the husband is heterozygous, the prognostic significance of the past history is partially invalidated. In regard to Dr. Potter's statement that "In no instance did a live born infant die whose birth had not been preceded by that of an infant with erythroblastosis," it seems to me that this announcement is likely to lead to unjustified optimism unless its implications are most carefully analyzed. It should be noted that she says: "In no instance did a live born infant die." She does not say that there were no cases of erythroblastosis and no stillbirths. This suggests that the statement may be more a reflection on the excellent therapy some of these infants received than any sweeping evidence in support of the prognostic value of a negative past history. Plausibility is lent to this suspicion when the author's statistics in the fifth paragraph of the above abstract are considered. Of the 178 infants delivered as the first child known to have erythroblastosis, 56 died before birth, 60 died after birth and 62 survived. Nevertheless, since in her later series of mothers with a history of a previous erythroblastotic child, only 2 babies could be saved, it would appear that a negative history does portend a much better outlook and a lesser degree of damage, if such occurs, than a positive history. This is forcefully brought out in the author's statistics in the second from the last paragraph above. Erythroblastotic infants whose mothers had a negative past history showed a mortality rate of 38 per cent, in contrast to a rate of 90 per cent in infants whose birth had been immediately preceded by the birth of an erythroblastotic baby. In other words, a negative past history possesses, in itself, a certain degree of relative prognostic import, but it would be hazardous to draw sweeping conclusions from this one circumstance alone. Here lies the auxiliary value of

antibody titer, provided it is negative. If the titer is zero with a negative past history, the outlook is almost 100 per cent good; and prognosis is most dependably established in these cases on the basis of such a history plus a negative titer. If the titer is positive, less definite conclusions can be drawn and in that case, as Dr. Potter stresses, the past history is a more dependable prognostic guide than titer levels or titer changes.—Ed.)

HEMOLYTIC DISEASE OF THE NEWBORN: CRITERIA OF SEVERITY

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Brit. M. J. No. 4594, 123, 1949

Hemolytic disease of the newborn may be diagnosed with certainty at the time of birth by the direct Coombs test (Lancet 1: 264, 1946). Since this test seems to be positive in all cases of hemolytic disease, further criteria are required to assess the severity of individual cases. In general it is agreed that a prognosis based upon antibody tests must be offered with reservations.

This paper presents evidence that the hemoglobin value of the cord blood is a satisfactory criterion of the severity of hemolytic disease in the newborn.

Sixty-nine infants having a positive Coombs test were studied; 52 healthy full-term infants were used as controls. Cord blood or venous blood was studied for hemoglobin content by the photoelectric method.

The cord blood of 52 normal infants had a mean value of 16.35 gm. %; in contrast, among 30 affected infants, 16 had values below the normal range, from 3.4 to 12.8 gm. %. There were 10 deaths among the 16 anemic infants.

The mean value of hemoglobin in the venous blood of 43 normal infants on the first day post-partum was 18.45 gm. %. Among 43 affected infants subjected to a similar test, 29 had values below the normal range, from 3.7 to 14.3 gm. %.

Capillary blood obtained from 33 normal infants on the first day showed an average value of 19.1 gm. %. In a similar way the capillary values of affected infants were distinctly higher than in the venous samples. Capillary blood samples usually give considerably higher values than venous samples and may mask anemia.

Affected infants having cord hemoglobin above 15.1 gm. % were not treated and all did well. An infant can have a positive direct Coombs reaction for one to two months post-partum without developing any significant anemia.

In 33 of 49 affected infants there were at least 20 nucleated red blood cells per 100 white blood cells. Fifteen of these infants died.

The mean value for cord bilirubin in normal infants was 1.6 mg. %. In affected infants, the values ranged from 1.0 to 9.3 mg. %; and above 4 mg. %, 50% of

the cases died. There is definite correlation between low hemoglobin and high bilirubin values.

The amount of free antibody (as determined by albumin titration) in the affected infants was not well correlated with clinical manifestations. Moreover, persistence of free antibody is not *per se* associated with tissue damage. Correlation between maternal Rh antibodies and the severity of the disease in the infants was poor.

In infants with severe or moderate anemia, the venous pressure was usually raised, the cord often bleeding violently when cut. A definite correlation was observed between low initial hemoglobin and death on the first day of life.

Very severe anemia at birth probably kills the infants by causing cardiac failure. Deaths 2 to 5 days post-partum are probably due to medullary failure consequent upon cerebral damage. Accordingly, it is the severity of the hemolytic process which determines the likelihood either of severe fatal initial anemia or later kernicterus. The cord hemoglobin is the most satisfactory criterion for determining the severity of the hemolytic process. Antibody titres, both in mother and infant, are unreliable. Infants whose cord hemoglobin is below 8 gm. % usually die within 24 hours after birth and do not have time to develop kernicterus. Infants with cord hemoglobin values of 10 to 12 gm. % may acquire values of 12-15 gm. % in venous samples taken a few hours after birth and capillary values may be as high as 18 gm. %. The infant's rapid production of cells does not fall off for 2 to 3 days after birth and therefore an infant whose hemoglobin value was 12 gm. % at delivery may die on the 3rd day with a hemoglobin of 16 gm. %. The latter value does lie within the normal range of hemoglobin values for the 3rd day of life but it is normal only for an infant which received little or no placental blood. In an infant which has received a large amount of placental blood, 16 gm. % in the capillary blood on the 3rd day of life indicates anemia.

The authors conclude that a cord hemoglobin taken at delivery is the most reliable index of the severity of the hemolytic process.

PNEUMONIA IN THE NEWBORN RESULTING FROM THE INHALATION OF GASTRIC CONTENTS

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Arch. Dis. Childh. 23: 116, 1948

The authors present a review of the pathological features of 41 cases of pneumonia resulting from the aspiration of gastric contents in the newborn.

The main pathological features include congestion of the mucous membrane and muco-purulent exudate in the lumen of the respiratory tree. Foreign material

was recognized only in early cases. Grossly, the lungs showed widespread consolidation and extensive areas of hemorrhage. Beads of pus and sometimes recognizable vomitus exuded from the bronchi. Emphysema and pleurisy were unusual.

Microscopically, heavy bacterial infection, desquamation of the bronchial epithelium, purulent exudate and massive alveolar hemorrhage were striking features. In the most advanced cases, foci of suppuration developed in and about the bronchi.

Bacteriologically, *B. coli* was the most frequent organism isolated.

The 41 cases in this study occurred in 962 autopsies on infants born alive during the period 1936 to 1939. Thirty-nine of the infants were less than one month old. During the last 2 years of the study 27 cases were observed compared to only 14 during the previous 5 years. This increase may be related to a shortage of nursing staff.

Clinically this pneumonia differs not at all from other types; 33 of the infants were premature (less than 5½ pounds), 25 died between the 4th and 9th day. In 26 of the cases pregnancy was normal. Delivery was spontaneous in 25 cases, 10 were delivered by forceps, 4 by breech extraction and 2 by section. Most of the infants who died during the first 4 days were in unsatisfactory condition at birth. Three infants had developed mental anomalies and 18 had intracranial hemorrhage. Ten infants were known to have vomited; in 9 cases the vomiting was probably of importance in the etiology of the pneumonia.

Aspiration of material from the mouth will be favored by insensitivity of the protective reflexes of the pharynx and respiratory tract. Prematurity, feebleness, deep sleep and narcosis, intracranial hemorrhage, and chilling are some of the factors known to depress the activity of these reflexes. Prematurity is often associated with several other of these factors and this probably explains the high incidence of aspiration pneumonia in premature infants.

THE ROLE OF MATERNAL ILLNESS DURING PREGNANCY IN THE ETIOLOGY OF MONGOLISM

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Am. J. Ment. Defic., 53: 2, 1948.

Three main theories have been advanced to explain the cause of Mongolism. The first theory emphasizes hereditary factors; the second, damage to the germ plasm (either paternal or maternal); and the third, noxious factors originating with the mother during pregnancy. Mongolism has been demonstrated not to be hereditary in the strict Mendelian sense. The higher frequency of Mongolism in homozygotic as compared with heterozygotic twins has suggested defective germ

plasm as an etiological factor; however, in most of the cases, this theory has been proven to be invalid.

On the other hand, noxious factors such as increased maternal age, physical exhaustion, rapid childbearing, and grand multiparity have received much credence as etiological factors in Mongolism. The influence of rubella upon the infant has aroused speculation as to the possible role of infectious disease in the etiology of Mongolism. Ingalls and Davies (*New Eng. J. Med.* **236**: 437, 1947) described 7 cases in which intercurrent maternal infection was thought to have been a factor in the production of Mongoloid children. However, they concluded that such an etiology would account for only a small fraction of the cases of Mongolism.

This study includes 75 Mongoloid children and a control group of 86 feeble-minded children. The feeble-mindedness of the control group was of unknown etiology. Questionnaires were sent to the families of the children studied. Specific inquiries were made as to maternal illness in pregnancy (with special regard to the first trimester), the age of the parents, the duration of marriage, order of birth, and the family history with especial regard to Mongolism and other nervous or mental diseases. Questionnaires were returned by 64 of the Mongoloid and 83 of the control group.

A positive family history of nervous and mental diseases occurred with equal frequency in both groups. A majority of the mothers of Mongolian children were over 35 years of age at the time of delivery. The same is true of the fathers. The majority of parents had been married more than 15 years. Of the 64 Mongolian children, 8 were only children, while 36 were last born, making 45 only and last children as compared with 19 children with other places in the birth order.

The incidence of intercurrent disease during pregnancy as a whole as well as in the first trimester was the same in both the Mongolian and the control groups.

The authors conclude that intercurrent infectious disease during pregnancy does not seem to have any effect upon Mongolism. On the other hand, this study appears to substantiate the belief that the ages of the parents and the birth order of the Mongolian child are of real significance in the etiology of this disorder.

RETROLENTAL FIBROPLASIA IN PREMATURE INFANTS

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Am. J. Ophthal., **32**: 1, 1949.

In 1942 Terry (*Am. J. Ophthal.* **25**: 203, 1942) described the formation of an opaque retrolental membrane in premature infants. In the fully developed case

there is an opaque, vascularized membrane against the posterior surface of the lens. The globe is often smaller than normal, the anterior chamber is frequently shallow, and occasionally posterior synechias form. Elongated ciliary processes, appearing like coarse teeth of a comb, can be seen behind the iris on the membrane in the extreme periphery of the dilated pupil.

Terry felt that the condition developed from a persistence and development of the connective tissue of the tunica vasculosa lentis; but he was unable to reproduce the disease by experiments upon the hyaloid system of opossums and rats. Reese and Payne (*Am. J. Ophthal.* 29: 1, 1946) felt that the condition was congenital and the result of persistence and hyperplasia of the primary vitreous. The latter was described as an angioblastic mesoderm that included the hyaloid system. Krause (*Arch. Ophthal.* 36: 387, 1946) thought that the disease was part of a "congenital encephalo-ophthalmic dysplasia," a generalized pathologic process characterized by retinal and cerebral hypo- and hyperplasia.

Prior to the present study, the development and course of retrolental fibroplasia had not been described, nor had the earliest stages been observed. This study covers all premature infants weighing 2000 gms. or less who were admitted to the premature nursery of the Johns Hopkins Hospital from July, 1945 to June, 1947. The babies were examined every month until they were 6 months old; and thereafter every other month until the age of one year.

One hundred and twenty children born during the period 1935-1944, who had weighed 2000 gms. or less at birth, were examined in an attempt to determine the incidence of the disease. None had retrolental fibroplasia. Twenty three of these infants had weighed less than 1360 gms. at birth.

From July, 1945 until June, 1947, 214 premature infants weighing 2000 gms. or less at birth, were examined. Forty of these weighed less than 1360 gms. None of these infants had retrolental fibroplasia at birth. One hundred and eleven of these infants, 33 of whom weighed less than 1360 gms. at birth, were followed for 6 months or more. Four of the infants weighing less than 1360 gms. developed retrolental fibroplasia (12.1%); one infant in the group weighing from 1360-2000 gms., developed the disease (1.3%). Thus, by far the greater incidence occurred in the very premature group of infants.

In numerous very premature infants, remnants of the posterior portion of the tunica vasculosa lentis and extensive pupillary membranes were seen at birth. In all cases these vessels disappeared. The authors observed the development of retrolental fibroplasia in 9 cases. In one case, early fundus changes appeared, but the disease then apparently regressed.

The course of development of the lesion was as follows: all visible remains of the hyaloid system disappeared early in postnatal life. On early observation the eyes appeared normal. The earliest detectable abnormality was a slight dilatation of the retinal arteries and veins. The veins then dilated to 3 times normal size; the arteries became very tortuous. The angiomatic dilatation and tortuosity were followed by grayish yellow elevations of the retina in the far periphery. Soon the margins of the disc became blurred and generalized retinal edema developed. The grayish masses in the retina increased in height, and other grayish yellow areas appeared scattered throughout the fundus. A gray membrane

with numerous vessels coursing over it billowed forward in folds at the periphery of the retrolental space. At this stage the fundus could be seen only hazily. Bands of tissue extended from the areas of detached retina into the vitreous. Between these bands a yellowish red fundus reflex was visible. Finally, a complete retrolental membrane was formed by gradual extension and fusion of the peripheral folds of the retina. Broad ciliary processes extended onto the periphery of the membrane and numerous vessels were present on its surface. Occasionally small hemorrhages occurred into the membrane from these vessels. The anterior chamber became shallow, posterior synechias formed and the iris developed a grayish atrophic appearance. Later, some of the eyes showed secondary changes with extension forward of the iris and lens and clouding of the cornea.

Not all infants passed through the complete development of the syndrome. In some, the disease became arrested at the stage of retinal edema, and then regressed, finally showing only a little grayish tissue about the margins of the optic nerves. Sometimes a complete retrolental membrane was formed, but glaucoma did not occur; later, in some cases, thinner areas appeared in the membrane.

In all cases the major manifestations of the disease occurred between the 2nd and 5th months of life. In no case did a retrolental membrane develop after 5½ months of life.

Terry proposed the theory that retrolental fibroplasia was due to arrest in growth or aberration of some embryonic or fetal structure. He believed that the lesion was a fibroplastic overgrowth of the hyaloid artery and tunica vasculosa lentis. However, in none of the cases presented was there a persistence or reopening of the hyaloid artery or of the tunica vasculosa lentis.

Reese and Payne believed the lesion was a persistence of the primary vitreous with or without hyperplasia. The authors found no evidence of abnormal embryonic structures and the earliest changes observed occurred in the retina and the retinal vessels.

The cause of the syndrome is unknown. It is possible that the vigorous vitamin and chemotherapy commonly given to premature infants may produce a metabolic imbalance which is related to the disease. The authors are at present attempting to evaluate these factors by a detailed study of the nursery records of the infants who developed retrolental fibroplasia.

It is possible that retrolental fibroplasia may be related to angiomas of the retinae or to Coats's disease. Hemangiomas of the skin appear more frequently in premature infants than in full-term siblings. Hess, Mohr, and Bartelme found that in a group of premature children, the hemangiomas were found among the children with low birth weights (under 2000 gms.).

(Since the demonstration by Terry in 1942 that this blinding disease affects a substantial proportion of small premature infants, the problem it presents has been of the greatest concern to ophthalmologists, pediatricians and obstetricians alike. Indeed, if some 20 per cent of 2 pound prematures are to become blind as the result of retrolental fibroplasia, as the early figures indicated, the question has even arisen as to the justification of extreme efforts to rear these small infants. The figure reported by the Owens' for the incidence of the dis-

ease in prematures under 1360 Gm. (3 lbs.) since 1945, namely 12.1 per cent, is somewhat less than that first reported; but even this incidence is large enough to cause concern.

Intensive efforts are being made by ophthalmologists to ascertain the etiology and prevention of this disease. Premature exposure to light has apparently been ruled out as a cause; and attention is now being directed to vitamin deficiencies, especially C deficiencies. The results of these studies will naturally be awaited with the greatest interest and hope.—Ed.)

CHANGES IN LENS OF EMBRYO AFTER RUBELLA. MICROSCOPIC EXAMINATION OF EIGHT WEEK OLD EMBRYO

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Arch. Ophthal., 36: 135, 1946.

Beginning with Gregg (Tr. Ophth. Soc. Australia 3: 35, 1942), congenital cataract has frequently been described following rubella in the mother during pregnancy. In 170 cases of rubella occurring during pregnancy, 125, or 73% of the children had congenital defects of the lens. In all of these cases the rubella occurred during the first 3 months of pregnancy. The present report deals with the examination of a single eye from an 8-week embryo in whose mother rubella was present.

The eye was obtained from a therapeutic curettage. It was serially sectioned at intervals of 6 microns. The surface epithelium was absent (artefact) and the lids did not cover the eye. The optic cup was well formed and the outer layer was fully pigmented. The retina and posterior portion of the eye showed development normal for a fetus of 19 mm. in length. The lens showed retardation, with distortion and disorientation of the cells at the anterior pole, failure of the primary fibers to completely fill the cavity of the lens vesicle, and uneven staining of the nuclei. There was vacuolation and early degeneration of the fibers at the anterior pole of the lens. The lenticular development was equivalent to an embryonic length of 17 mm.

In the normal eye, the cavity of the lens vesicle is obliterated by the 6th week. In the present specimen, a remnant of this vesicle remained, indicating that the action of the toxic agent had occurred about the 6th week of embryonic life.

Swan (J. Path. & Bact. 56: 289, 1944) studied the pathologic changes in 3 infants who died of congenital defects. The mothers of the infants had all had rubella early in pregnancy. He found necrosis en masse of the nuclear portion of the lens. Both the primary and secondary lenticular fibers were involved, indicating that the action of the noxious agent persists after the 7th to 8th week of pregnancy, since the secondary fibers are not formed until after that time.

The embryo might be affected by a theoretical noxious agent in 2 ways:

either through the cord, or by direct contact of the eyes with the amniotic fluid. At the time the virus presumably acted on this specimen (the 6th week), the lids had not covered the eye, nor had Descemet's or Bowman's membranes been formed. The protection afforded by these structures after the 3rd month might explain the declining frequency of congenital cataracts in rubella contracted after that time.

(Observations such as this, as they accumulate, should greatly enlarge our knowledge of the precise time when rubella affects the embryonic eye and how.—Ed.)

DEATH OF A NEWBORN INFANT FROM INTRATRACHEAL INSUFFLATION

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Am. J. Dis. Child., 77: 76-81, (Jan.) 1949

The case is reported of a premature baby boy who was born by spontaneous normal delivery and was lethargic after birth. He took only a few gasps at birth and was considered to have asphyxia pallida. A tracheal catheter was inserted under direct vision and connected to the oxygen outflow of a Kreiselman-Moxel-Heidbrink resuscitator which was set to flow at 7 liters per minute. Almost instantly the baby was noticed to stiffen, the abdomen became distended, subcutaneous emphysema was noted and the heart beat stopped. At autopsy the infant was found to have interstitial emphysema of the right lung, posterior pneumomediastinum, emphysema of the deep fascial layers of the neck, right pneumothorax, pneumopericardium, pneumoperitoneum, tamponade of the large veins and congenital atelectasis of the left lung. It was felt that the accidental use of excessively high pressure of 300 mm. of Hg. was responsible for the lesions which were seen.

With increased intrapulmonary pressure there is overdistention of the alveoli with minute rupture of their walls. The air enters the perivascular sheath and lymph channels and travels toward the hilum and thence to the mediastinum. From there, it follows the course of least resistance to the other portions of the body.

The pressure required to produce emphysema and pneumothorax via the pulmonary passageway is between 18 and 40 mm. Hg. whereas it requires 80 mm. Hg. pressure to rupture a bleb on the surface of the lung. The maximum pressure for safe resuscitation of the newborn is slightly less than 18, or approximately 15 mm. Hg. The writers stress the importance of mediastinal emphysema as a cause of circulatory tamponade and suggest the use of mediastinal aspiration as an emergency procedure.

(Having used the Kreiselman resuscitator for 14 years in hundreds of cases without an accident or near-accident, I feel impelled to point out that the tragic case reported can in no wise be charged against the apparatus. As a safeguard against such accidents, the face mask which is supposed to be used with the oxygen flow-meter and which is an integral part of the apparatus, contains a hole in it as big as a quarter. Hence, no pressure whatsoever can be built up in this mask which is designed for use only with breathing infants to give them more oxygen than is contained in air. In the above case the apparatus was apparently dismantled, the mask removed and the catheter connected directly with the flow-meter. This is tantamount, of course, to connecting it directly with the tank of oxygen.—Ed.)

PREVALENCE AND DISTRIBUTION OF OSSIFICATION CENTERS IN THE NEWBORN INFANT

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Am. J. Dis. Child., 77: 355, 1949.

A total of 1,112 newborn infants (298 white boys, 267 white girls, 271 Negro boys and 276 Negro girls) were observed. No multiple births or syphilitic infants were included, and all infants were in sufficiently good condition to warrant an x-ray examination of their long bones within 72 hours of birth. X-rays were taken and read for the presence or absence of ossification centers in the calcaneus, talus, cuboid bone, third cuneiform bone, distal epiphysis of the femur, proximal epiphysis of the tibia, capitatum, hamate bone, head of the humerus and head of the femur. The data for the presence of these centers were analyzed in relation to birth weight, sex and race.

It would appear that the order of appearance of the ossification centers is as follows: calcaneus, talus, distal epiphysis of the femur, proximal epiphysis of the tibia, cuboid bone, head of the humerus, capitatum, hamate bone, third cuneiform bone and head of the femur. The centers of the distal epiphysis of the femur and the proximal epiphysis of the tibia are of clinical importance, since it has been known that the former appear 6 weeks before term, thus indicating physiologic maturity. In the groups with weight of less than 2,000 gm., the distal epiphysis of the femur was present in 9.1% of the white boys, 50% of the white girls, 18.2% of the Negro boys and 50% of the Negro girls. In the 2,000 to 2,499 gm. weight groups, the distal epiphysis of the femur was present in 75% of the white boys, 91.7% of the white girls, 88.5% of the Negro boys, and 93.8% of the Negro girls. In the 3,000 to 3,499 gm. weight group, the distal epiphysis of the femur was present in 85.3% of the white boys, 98% of the white girls, 90.7% of the Negro boys, and 99% of the negro girls.

In the groups of weight of less than 2,000 gm., the proximal epiphysis of the tibia was not present in any white boy, white girl or Negro boy, but was present in 14.3% of the Negro girls. In the 2,000 to 2,499 gm. group, the proximal epiphy-

sis of the tibia was present in 18.8% of the white boys, 54.2% of the white girls, 38.5% of the Negro boys, and 40.6% of the Negro girls. In the weight group of 2,500 to 2,999 gms., the proximal epiphysis of the tibia was present in 52.9% of the white boys, 75.5% of the white girls, 62.7% of the Negro boys, and 76.7% of the Negro girls.

For any selected center of ossification in infants of either race or sex, there is progressive prevalence as the weight at birth increases. For each center of ossification in each of the weight groupings, greater prevalence was noted in the Negro girls than in the Negro boys and in the white girls than in the white boys.

With a thorough knowledge of the development of the osseous pattern in the newborn, and with better technics for visualizing fetal parts, it is possible that much information can be gained in utero concerning the relative osseous and physiologic maturity of the infant. At the same weight level, Negro infants are physiologically more mature than white infants, and female infants of either race are more mature than male infants.

LIVER FUNCTION IN NEWBORN INFANTS WITH SPECIAL REFERENCE TO EXCRETION OF BROMSULPHALEIN

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Arch. Dis. Childh., Lond., 24: 12, 1949.

Direct evidence that the liver in newborn infants is unable to function adequately is scarce and somewhat contradictory. Increasing emphasis has been placed on the role of the liver in the genesis of neonatal jaundice.

Bromsulphalein excretion tests were performed on 83 normal full-term infants. The infants were between 8 and 216 hours old. In 32 infants from one to 7 days old, thymol turbidity and thymol flocculation, cephalin cholesterol flocculation, and colloidal gold tests were performed. Serum bilirubin levels were measured in most of the infants in both groups.

During the first 4 days of life most of the babies showed more retention of the dye than did babies of 4 to 9 days of age. Babies of 4 to 9 days showed more retention than that regarded as normal for healthy adults. There was no correlation between the results of the bromsulphalein tests and the levels of serum bilirubin. There was no correlation between the retention of dye and the weight of the babies. Thymol turbidity and thymol flocculation tests, cephalin cholesterol flocculation tests, and colloidal gold tests showed no abnormality whatever.

The results of the bromsulphalein tests are in general agreement with those of Herlitz (1927) who found poor excretion in the youngest infants and no correlation with the presence or absence of jaundice. The cause or causes of the retention of the dye may be related to circulatory adjustments taking place in the

first days after birth. In view of the negative results with the other tests, it seems unlikely that the liver cells are damaged. The continued poor excretion of the dye after the first 4 days suggests that the liver may be "immature" as regards its excretory function, but the rapid improvement in the first few days makes it appear that some other factor is also involved.

(The same conclusion was reached by Hazel Lin and myself on the basis of bilirubin excretion curves (*Am. J. Obst. & Gynec.* 1937, 33: 317). The ability of full term newborn to excrete bilirubin was found to be normal and no different in babies who developed jaundice than in those who did not. As the authors point out, some other mechanism must be involved.—Ed.)

OPERATIVE OBSTETRICS

POSTMORTEM CESAREAN SECTION AFTER DEATH FROM BULBAR POLIOMYELITIS: REPORT OF TWO CASES WITH LIVING INFANTS

J. M. SIMMONS, JR. AND H. B. ELLIS

University of Colorado Medical Center, Denver, Colorado

Am. J. Obst. & Gynec., 57: 603-605, March, 1949

The poliomyelitis epidemic in Colorado in 1946 revealed that pregnant women were twice as susceptible to this disease as their non-pregnant sisters. During the same epidemic the mortality rate in the last trimester of pregnancy was 50 per cent. In view of these appalling statistics, the following 2 cases are reported to demonstrate that a living fetus can be delivered even though the mother might perish.

The first case was that of 31-year-old white gravida viii, para vii, who was admitted in her seventh month of pregnancy with vomiting, pains in the neck and numbness and tingling in her left hand. One of her children had died of poliomyelitis 9 days prior to this admission. She was found to be quite sick on examination, with dyspnea, orthopnea, nuchal rigidity, weakness of the left arm, inability to swallow and cyanotic extremities. The use of the accessory muscles of respiration was required for breathing. The patient's course went steadily downhill after admission with increasing cyanosis and difficulty in breathing. Within 6½ hours she became moribund and immediately at death a cesarean section was performed. Twin boys were delivered, one of which lived for 12 days and then died of atelectasis. The other child made no respiratory effort. Postmortem examinations showed clear-cut evidence of bulbospinal poliomyelitis in the mother but neither of the infants showed any evidence of that condition, though changes secondary to anoxia were present.

The second case was a 23-year-old gravida iii, para ii, who was admitted at the eighth month of pregnancy complaining of headache, aching in the neck, diarrhea and generalized weakness. The spinal fluid findings were compatible with poliomyelitis. After 48 hours in the hospital, the patient began to show some respiratory distress and so was placed in a respirator. There was no change in her condition for the next 5 days, and then she began to go rapidly downhill. The temperature was elevated, coma developed and she went into pulmonary congestion and died. An immediate cesarean section was performed and a living female infant was delivered. She was slightly cyanotic at birth but this disappeared and the child developed normally. Postmortem examination of the mother showed diffuse central nervous system involvement with the poliomyelitis virus.

(Poliomyelitis is one of the few diseases in which there is reasonable hope of obtaining a living child at postmortem cesarean section because the virus shows such an affinity for nervous tissue that it does not accumulate in the maternal blood and so does not reach the fetus.

Postmortem cesarean section is undoubtedly the oldest form of the operation, its history extending back to mythological times. Thus, Dionysus, the youthful, beautiful, but effeminate god of wine, was born, according to one legend, in this fashion. Similarly, Aesculapius was so born, his mother, Coronis having been burnt on a funeral pyre after which Artemis opened her abdomen and withdrew him. The idea possibly arose from observations made on pregnant animals which had been sacrificed or killed in the hunt.

In this connection it will be recalled that even the name of the operation probably stems from the fact that in ancient Rome postmortem cesarean section was mandatory. Under Numa Pompilius (715-672 B. C.), the Lex Regia forbade any pregnant woman to be buried before delivering the infant through the abdomen. Under the emperors this law became the Lex Caesarea and subsequent historians have read into this circumstance the assumption that the operation was known as the Caesarean operation. The Christian Church in the West approved of the procedure because it permitted the baptism of a possibly living child.

To-day postmortem cesarean section is approved by some obstetricians while others question its justification. In the latter group, Dr. Williams, as stated in his textbook, resorted to it only at the urgent request of the family because so few babies are saved and because of the abhorrence in which the laity hold it. Provided the consent of the husband can be obtained, I believe it should be performed but, as is well known, the yield in terms of surviving infants will be small.—Ed.)

SOME OBSERVATIONS ON THE AFTERCOMING HEAD

J. BAXTER

Rankin Maternity Hospital, Greenock, Scotland

J. Obst. & Gynaec. Brit. Emp., 56: 95-106, February, 1949

This paper deals with some aspects of breech delivery not over-emphasized in the literature. The aftercoming head can present a formidable problem, no matter how it be approached. The frequency with which the aftercoming head gives rise to difficulty is not easy to determine, but in the writer's series of 85 consecutive cases of fulltime uncomplicated breech labor in primigravidae, there were 6 cases of difficult labor due to the aftercoming head. These resulted in 3 stillbirths and one case of Erb's paralysis which responded to treatment.

There were also in this series 2 stillbirths and 2 neonatal deaths not associated with difficult delivery. There was no maternal death. Puerperal sepsis of low virulence occurred in 2 cases. The smallest infant weighed $5\frac{1}{2}$ pounds, the heaviest 9 pounds, and the average weight was 6 pounds, 14 ounces, or about 1 pound less than average for full-time vertex presentations over the same period. The weights of the stillborn fetuses and of infants dying in the neonatal period show that weight of the fetus is probably not a factor contributing to fetal loss in this series. Although the fetal weight as it rises above 9 pounds becomes an increasingly

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dangerous factor in the development of dystocia, it is chiefly because great bulk of the thorax predisposes to extension of the arms, and also prevents access to them so that they cannot be dealt with in the time available. The head of a 10-pound baby usually shows an increase of about 1 inch in the sub-occipito-bregmatic circumference and $\frac{1}{4}$ inch in the related diameters when compared with the average 7-pound baby, but such a difference is well within the margin of pelvic safety. It is obvious that the size of the normal fetal head can rarely, if ever, be a determining factor in dystocia during breech labor, provided the head engages fully flexed. Neither does plasticity of the fetal head appear to be of importance as an etiologic factor in aftercoming head dystocia, and it is suggested that nothing is to be gained by induction of premature labor because of breech presentation, except in a few carefully selected multiparae to avoid a very large fetal bulk. The size of the normal fetal head only becomes a factor in respect to its attitude.

The central factor in any of the various techniques for dealing with the aftercoming head is derived from the necessity of obtaining and maintaining head flexion, and suprapubic pressure plays a part in most of them. The fetal head moves at the atlanto-occipital joint and the old concept of this joint representing the fulcrum of a head lever with a long anterior and short posterior arm gives an excellent mechanical representation. Suprapubic pressure may fix the head so that it is incapable of following the direction which the forces of labor give to it. It would seem to be important that the attendant know the position of the fetal head, so that suprapubic pressure can be exerted where it is most advantageous. When the head engages with the occiput directly anterior it would seem sounder technique to make upward pressure upon it and so aid flexion.

It is estimated that the limit of safe traction force on the shoulders is probably between 30 and 40 pounds. The use of greater force than this results in rupture of blood vessels in the base of the brain and a "pressure-cone" effect on the medulla. The power of the expulsive forces in the second stage has been estimated to be about 46 pounds of maximal total force, and it would therefore seem that when the patient is unable to expel the head by spontaneous effort of normal magnitude, shoulder traction is unlikely to deliver a live infant.

It has long been recognized that forceps delivery of the aftercoming head has great advantages over jaw flexion and shoulder traction. Forceps promote flexion of the aftercoming head only if the blades are accurately applied to the sides of the head and the instrument one which allows traction in the pelvic axis. When the axis traction instrument is accurately applied, dangerous compression effects are not likely to develop before traction has reached about 70 pounds.

Real mechanical obstruction such as occurs with extension of the head above the brim usually requires general anesthesia with complete relaxation if it is to be adequately dealt with. Using ethyl chloride followed by open ether 10 minutes or longer may be required to obtain relaxation. It is possible that quick-acting anesthetics such as cyclopropane or sodium pentothal may be useful in these cases. Faced with the necessity of forcing the issue or abandoning the fetus to asphyxia during induction to allow safer delivery of the mother, the writer has occasionally kept the fetus alive by introducing an airway into the mouth.

Finally, the author discusses external version as a means of eliminating breech labor from practical obstetrics. It is concluded that in those schools where the figures for breech delivery are comparable, or nearly so, with those resulting from vertex labor, version may be regarded as carrying a greater risk than breech labor itself. For many of us, however, version when it can still be performed is the best solution to the problem. 5 figures.

(As the author stresses, maintenance of flexion is one of the keynotes to success in the management of the aftercoming head. The great master of breech extraction, Irving W. Potter, used to emphasize this and gave the following advice: (1) prior to delivery of the shoulders, no pressure should be exerted on the abdomen since this pushes the head downward and allows the arms to come up and the chin to extend,—complications which must be avoided if at all possible; (2) after the arms and shoulders have been delivered, gentle pressure in a posterior direction should be made on the occiput just above the occiput to increase flexion. As pointed out by Baxter, the direction of this pressure might well be posteriorly and slightly upward. Visualization of the aftercoming head with the occiput anterior will make it clear that pressure in such direction is best designed to promote flexion; (3) proceed slowly and gently since there is no hurry,—one of Potter's greatest contributions. Although Potter rarely employed it, the advantage of forceps to the aftercoming head is now well established.—Ed.)

A NEW CONCEPT IN THE REPLACEMENT OF THE INVERTED UTERUS AND A REPORT OF NINE CASES

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Am. J. Obst. & Gynec., 57: 557-562, March, 1949

The author describes his method of replacing the inverted uterus, based on placing the ligaments of the pelvis on tension to aid in returning the fundus to its normal position. He points out that dimpling of the fundus is often unsatisfactory. As the uterus becomes inverted the ligaments follow the fundus through the pelvic outlet and they are not altered in tension or length by the inversion *per se*. To replace the uterus, he advises that the entire hand be placed in the vagina with the tips of the fingers at the uterocervical junction and the fundus in the palm of the hand. The entire uterus is then lifted out of the pelvis and forcefully held in the abdominal cavity above the level of the umbilicus. This puts tension on the ligaments which are so situated as to cause widening of the cervical ring and then to pull the fundus through the ring. The fundus should be held in this position for 3 to 5 minutes in which time it can be felt receding from the palm.

This method of replacement is simple and can be done immediately without increasing shock and, as a matter of fact, the author states that shock and hemorrhage are relieved by the procedure. Nine cases are reported in some detail. General anesthesia is necessary and was used in all these cases. Six patients were primigravidas. The ages ranged from 19 to 30 years. Eight of the cases showed

marked hemorrhage and shock, and blood and plasma were given in all such cases. The one case which was not in shock was diagnosed immediately and the uterus was replaced within 6 minutes. In 7 cases the third stage of labor lasted 31 minutes or less, in one case 70 minutes and in another 2 hours and 13 minutes. In 6 cases the period of inversion was short, varying from 6 minutes to 5 hours and 35 minutes. In one case the period of inversion was 14 days, in another 2 months and in a third, 3 months. In 2 cases subsequent pregnancies were uneventful. There was no mortality and all of the cases showed normal involution of the uterus following replacement. 4 figures.

EXTRAPERITONEAL CESAREAN SECTION IN THE PROFOUNDLY INFECTED PATIENT

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Am. J. Obst. & Gynec., 57: 520-531, March, 1949

It has been estimated in recent years that at least 38 per cent of all cesarean section deaths are due to infection. The majority of these are due to peritonitis and follow operations of the transperitoneal type. The fact that each succeeding hour of labor, ruptured membranes or a combination of the two increases the probability of intrauterine infection has caused modern clinics to attempt to manage cases with this in mind. A list of the contraindications to the transperitoneal cesarean section should include the following: labor over 24 hours, ruptured membranes over 24 hours, attempts at delivery by forceps or version, induction of labor by bag, bougie or pack, evidence of uterine infection, more than 6 vaginal examinations, more than 12 rectal examinations, and dead or damaged fetus. There is controversy over the proper management of these cases, with one group advocating embryotomy or cesarean hysterectomy and the other group extraperitoneal cesarean section. The author believes that the latter procedure is the one of choice in most of these cases.

The author has reviewed 3 series of cases in which the extraperitoneal approach was employed. There were 91 cases in the combined series. There was no maternal mortality and the fetal mortality was 8.8 per cent. All of the cases presented one or more of the factors described as contraindications for transperitoneal cesarean section.

The author also reports in detail 18 of the more severely infected patients, and in none of these was there a maternal death. He points out that transperitoneal cesarean section in infected cases is dangerous even though advantage is taken of the modern antibiotics and chemotherapeutic agents. Difficult embryotomy is pictured as being outmoded and reprehensible. Cesarean hysterectomy is criticized as being mutilating and a dangerous procedure when used in primigravidas,

even though severe uterine infection is present. The modern technique of extra-peritoneal cesarean section is the safest and simplest method of treating severely infected cases when vaginal delivery of an intact infant cannot be consummated.

(The full import of this article can only be obtained by reading the case histories of the 18 gravely infected patients. This report is one of the most forceful testimonials in support of extraperitoneal section I have seen and the author deserves congratulation not only on this score but also because he managed to save all these desperately sick women.—Ed.)

CAESAREAN SECTION IN DUBLIN

J. K. FEENEY

Irish J. M. Sc., 6: 755, 1948.

The author analyzed 2,273 primary and repeat cesarean sections performed in the 3 Dublin lying-in hospitals from 1932-1946. There were 1,415 primary sections with a maternal mortality of 3.5% and a fetal mortality of 14.3%: the 858 repeat sections showed a maternal mortality of 1.4% and a fetal mortality of 6.7%. The rates are based upon intern deliveries only; all modes of abdominal delivery are included. The section rate has increased threefold as compared with a decade ago; from 1% to 3%.

The maternal mortality rate in cesarean section is 2%, at least 10 times that following all vaginal deliveries. The author suggests that attention be paid to the following points in the endeavor to reduce maternal fatalities: (1) antenatal care resulting in early recognition and admission to the hospital of patients requiring section, thus reducing the emergency admissions, (2) genuine indications for section, (3) proper selection of anesthesia, (4) lower segment operation should always be performed, (5) early postoperative ambulation, and (6) modern methods for combating shock, hemorrhage and infection.

In primary sections, the fetal mortality rate was 14%. Reduction of fetal mortality embraces such broad considerations as early antenatal recognition and conservative treatment of toxemias and placenta previa, specialized care of cases of disproportion, proper anesthesia, avoidance of trauma to the fetal head during operation, treatment of asphyxia, anoxia and birth shock, the prophylaxis of neonatal infection and the management of premature infants.

The indications for section were (1) disproportion, (2) placenta previa, (3) toxemia, (4) uterine inertia, (5) tumors and other causes of obstruction, (6) maternal and fetal distress, (7) heart disease, (8) rupture of the uterus, (9) age, (10) previous operations, (11) abnormal presentations, (12) miscellaneous.

The relative advantages and disadvantages of induction of premature labor in order to avoid major disproportion in a primigravida on the one hand and of trial labor at term on the other are well known. In the cases cited, only those cases with gross contraction had elective sections for disproportion. Induction was carried out on 240 cases; 102 primigravidae and 138 multigravidae. In the

primigravidae 3 sections were necessary after induction; there was no maternal death and the total fetal loss was 7%. In the multigravidae, one section proved necessary, there was one maternal death and the fetal loss was 6%.

There were no maternal deaths in the elective sections. Of the 49 deaths in primary sections, disproportion was the major indication in 15 cases: 13 had been in labor before admission, one had had 12 hours trial labor, and one with complicating heart disease had started labor when section was performed. Of the 12 repeat section fatalities, 7 had elective section for disproportion. It would seem that elective first section for disproportion is safer than elective repeat section.

Placenta previa was the indication for section in 12.5% of the primary sections and in 0.6% of the repeat sections. In central placenta previa with a viable baby of reasonable size, section is the treatment of choice. During the 6 years 1942-47, 247 cases of proven placenta previa were treated in one Dublin hospital with one maternal death. The total fetal loss in 1942 was 62.5%; the loss for 1947 was 13.9%. These results may be attributed to early hospitalization, expectant treatment, the employment of lower segment section and the administration of blood.

Cesarean section in pre-eclamptic toxemia was considered as the mode of delivery under the following circumstances, (1) onset of signs of imminent eclampsia, (2) presence of albuminuric retinitis or retinal hemorrhages, (3) when it became apparent that the persistence of long-continued elevation of blood pressure would lead to chronic hypertension, (4) unsuitability for induction because of undilated cervix, (5) when the patient was an elderly primigravida, (6) when the baby was not of sufficient size to withstand trauma of a long labor.

In 39 cases, heart disease was the indication for primary section; in 6 additional cases, it complicated disproportion. In 11 cases, heart disease was the indication for repeat section. Five maternal deaths occurred in new sections and one in repeat section, a mortality of 10%.

Rupture of the uterus is best treated by laparotomy, extraction of the fetus and hysterectomy. In occasional cases where preservation of the uterus is of importance, repair of the rent may be undertaken in clean cases. There were 36 cases of rupture of the uterus with a maternal mortality of 14%.

Previous myomectomy is not necessarily an indication for section. The number, position, extent and depth of the myomectomy incisions; whether or not the endometrial cavity was opened; the presence of fever in convalescence; the probable site of the placenta in relation to scars; the age of the patient must be considered. The course of labor should be carefully observed and facilities for abdominal operation should be readily available. In the case of procidentia treated by vaginal plastic operation and followed by pregnancy, cesarean section should be considered.

There were 148 cases of vaginal delivery after previous section with no maternal deaths.

With an ideal obstetrical service fewer patients would require cesarean section and those who would require it would be in good condition. The author suggests: (1) induction of labor be given a trial in selected cases of disproportion,

(2) test labor be conducted only under hospital conditions, (3) conservative methods of treatment be continued in minor degrees of placenta previa, (4) the employment of section in toxemia should not be extended without full consideration of the maternal and fetal results now being achieved, (5) patients with heart disease usually stand the strain of pregnancy and labor, (6) some obstructing pelvic tumors may be displaced or aspirated, and (7) in many cases manual correction of abnormal cephalic presentation gives satisfactory results.

SUPRAVESICAL EXTRAPERITONEAL CAESAREAN SECTION: THE SECTION OF CHOICE FOR THE INFECTED PATIENT

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South. M. J. 42: 153, 1949

The most persistently recurrent cause of death following cesarean section, since the first operation was performed, has been peritonitis. Peritonitis may be caused by contaminated amniotic fluid in the peritoneal cavity at the time of section or by subsequent leakage of infected material through the uterine incision into the peritoneal cavity. The two operations most effective in preventing peritonitis are extraperitoneal cesarean section and cesarean hysterectomy.

The authors believe that supravescical extraperitoneal section is the operation of choice in the potentially infected or actually infected patient. The operation minimizes the development of peritonitis, is less shocking to the patient than hysterectomy and it conserves the uterus.

In 2,045 cesarean sections done in all hospitals in Jefferson County, Alabama, over a 16 year period, 72 deaths occurred (3.5% mortality). The majority of these deaths occurred prior to the advent of antibiotics. From 1945-1948, 3,205 sections performed in all hospitals in Alabama had a mortality rate of 0.96%. In both series, classical or low cervical sections were performed. The antibiotics are largely responsible for this improvement, but more frequent use of blood transfusion, continuous intragastric suction, continuous oxygen therapy and maintenance of fluid balance play an important role in the lowering of mortality.

The authors report 21 cases delivered by extraperitoneal cesarean section. The operation was essentially that described by Waters (*Am. J. Obst. & Gynec.* 39: 423, 1940). The indications for section were: previous section in 5 cases, disproportion in 13 cases, dystocia in 2 cases, and abruptio placentae in one case. Four cases were actually infected, 12 were potentially infected and 5 were uninfected. The bladder was injured in 3 cases, the peritoneal cavity perforated in 7 cases. There was one death in the series. The authors feel that this fatality was due to faulty operative technic.

CARDIAC INDICATION FOR THERAPEUTIC ABORTION

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Univ. Toronto M. J., 26: 219, 1949

The cardiac constitutes less than 2% of obstetrical admissions. If, on clinical evidence, continuation of pregnancy constitutes an unreasonable risk to the life of the patient, or if it jeopardizes her future health, consideration must be given to therapeutic abortion.

Generally, the prognosis in terms of maternal mortality is good if pregnancy occurs at an early stage of the patient's heart disease, and is bad in the late or terminal stage of that heart disease. So infrequent are other forms of heart disease that the problem may be studied from the standpoint of rheumatic heart disease alone.

The clinical factors of major importance influencing the stage reached by the patient in her heart disease are heart failure and serious disorders of rhythm. Those of minor importance are exercise tolerance, size of the heart, age, and valvular disease.

If heart failure has occurred in the normal state, the patient has reached a late stage of her disease and the prognosis is poor, and pregnancy will result in the patient's death or serious deterioration of her cardiac status. If unprovoked heart failure appears during the early months of pregnancy, it may become steadily worse until the circulatory burden reaches its maximum.

Patients with auricular fibrillation have a high mortality rate in pregnancy. There is a co-relation between exercise tolerance and occurrence of failure. The care the patient receives during pregnancy is of greater importance than the exercise tolerance, provided the patient remains within her tolerance. It is now agreed that the size of the heart is of little value in determining a patient's course in pregnancy. For the favorable cardiac, the safe period for childbearing lies between the ages of 23 and 35. On reviewing 340 cases of heart disease in pregnancy, Bramwell found the death rate in primiparae almost twice that among multiparae. With advancing years, cardiac status is likely to deteriorate and it is likely that it is age rather than parity which adversely affects maternal risk. Maternal death rate is little affected by the form of valvular disease present. Pregnant cardiacs with serious co-existing disease have a relatively high mortality rate. The cardiac patient with pre-eclampsia has an unfavorable prognosis.

Cases of heart disease in pregnancy may be divided into 2 groups: favorable and unfavorable. The unfavorable cardiac is the patient who has reached a late stage of heart disease. It has been shown that these patients run an unreasonable risk in becoming pregnant or when pregnant, if the pregnancy is allowed to continue. In the unfavorable cardiac, termination of pregnancy should be advised. The patient should be advised as to the facts in her case and be allowed to make her own decision. There is no absolute indication for termination of pregnancy in any cardiac patient.

In 200 cases of heart disease, termination of pregnancy before the period of viability was performed in 30. Twelve patients who had had cardiac failure before becoming pregnant or who developed it during the early months, had pregnancies terminated after recovery from the failure. Seventeen patients had pregnancies terminated because of marked impairment of exercise tolerance. Each case was carefully considered and the problem discussed with the patient. Every effort was made to carry the primiparous patient to term.

Termination of pregnancy or the induction of premature labor because of heart disease is rarely justified after the 28th week. By this time the maximum burden of pregnancy on the heart has been reached.

In 128 consecutive cases of heart disease, cesarean section was performed in 3 cases, all for obstetrical indications. Heart disease is not an indication for cesarean section.

(This and the succeeding 5 articles comprise a symposium on the indications for therapeutic abortion and set forth the viewpoints of the Toronto group on this important and controversial question. In general the recommendations are well-tempered and in keeping with the policies of most obstetricians.—Ed.)

TERMINATION OF PREGNANCY; ROMAN CATHOLIC VIEWS

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Univ. Toronto M. J., 26: 231, 1949

In a consideration of therapeutic abortion, one must begin with the mother. There are examples, however, in which a pregnancy may be terminated at a time when the fetus may be viable. This period is from 26 weeks to term, if the hospital has all the modern apparatus that facilitates the viability of the fetus. An induction of labor is quite permissible after this period.

If the life of the mother is at stake and abortion is essential to her welfare; as for example, in a case of uterine cancer, the act is indicated and permissible. It is true that the life of the fetus is lost, but one is doing something which is good for the mother, and if an undesirable effect is also obtained, it was not intended. The Roman Catholic Church does not sacrifice the mother for the child.

In the case of ectopic pregnancy, moral law recognizes that such a condition of the tubes is a pathologic one, and as such may be removed. The removal of the fetus in this instance is comparable to its removal if contained in a cancerous uterus.

The Catholic principle is that the life of the mother is as paramount as the life of the child. It is not approved to make a direct attack on the fetus to destroy it in order to save the mother. One is, however, justified and, in fact, urged to treat and save the mother and at the same time try to save the fetus and, therefore, both.

THE QUESTION OF THERAPEUTIC ABORTION IN
PULMONARY TUBERCULOSIS

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Univ. Toronto M. J., 26: 224, 1949

There is general agreement that pregnancy should be avoided in a tuberculous woman until the lesion has been inactive or quiescent for at least 2 years. If a childless tuberculous woman greatly desires pregnancy, she should be allowed to attempt it. The course of action to be taken when an already pregnant woman is found to be tuberculous is more questionable.

During the first trimester, if the tuberculosis is inactive, there is no particular problem. If it is active, the patient should be watched carefully in a sanatorium or hospital. If the disease is rapidly progressive and the patient toxic, the pregnancy may need to be interrupted. However, this is not often necessary; in a representative series of 118 cases, abortion was required only 4 times.

If the patient is seen for the first time during the second trimester, she should be treated with the same methods which are used in the non-pregnant patient. The pregnancy should not be interrupted at this time. During the third trimester, the pregnancy should be allowed to continue. If, in spite of sanatorium treatment, the tuberculosis becomes fulminating, the pregnancy should be terminated by section.

If open tuberculosis exists in the mother, lactation should not be permitted. Individualization of management and constant consultation between obstetrician and phthisiologist are mandatory.

If therapeutic abortion is to be employed in pulmonary tuberculosis, it should not be considered after the third month. After that time, it is at least as serious as delivery at full term and probably more so.

THE TERMINATION OF PREGNANCY

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Univ. Toronto M. J., 26: 217, 1949

The artificial termination of a pre-viable pregnancy is the gravest decision that one human being is called upon to make for another. The two indications which justify therapeutic abortion in the eyes of the law are the preservation of maternal life and the prevention of serious impairment of maternal health.

Domestic and economic conditions do not justify abortion. Although one

should not be indifferent to the invalid and underprivileged mother with too many children, her state does not justify the destruction of life. The state must adjust the economic factors at fault.

Termination of pregnancy on other grounds, such as the statistical probability of damage following German measles, the aggravation of otosclerosis already present, and the statistical probability of the development of erythroblastosis fetalis is not justified. These conditions do not involve maternal chances for survival. Moreover, exceptions to the statistical probabilities occur.

Psychiatric indications for abortions may be valid. Nevertheless, it may be possible for a shrewd malingerer to obtain an abortion in this manner.

During the first trimester, early abortion may be performed vaginally. From the 4th month until the cervix is ripe, abdominal hysterotomy is to be preferred, because labor may not follow rupture of the membranes. If the child has reached 28 weeks of gestation, it may not necessarily be lost.

The indications for termination of pregnancy may be divided into entities primarily due to the pregnancy and those incidental to it. The first group comprise the toxemias, the hemorrhages, and the diseases of the ovum. In this group of conditions, the obstetrician must make the primary decision. In the group with hemorrhage, many infants can be carried to term or at least to viability if a good blood bank is available.

In the conditions incidental to pregnancy, — the diseases of the mind, heart, lungs, kidney, and diabetes mellitus — the obstetrician must rely upon the specialized knowledge of the internist. However, the obstetrician is the agent and he must face the risks to the mother which are inherent in the operation. It is hoped that the internist recommending interruption of pregnancy will realize the responsibility of the obstetrician.

THE PSYCHIATRIC INDICATIONS FOR TERMINATING PREGNANCY

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Univ. Toronto M. J., 26: 229, 1949

Quantitative data are few in the psychiatric evaluation of a patient. Furthermore, the observer's judgment is unavoidably weighted by moral or ethical attitudes.

The psychiatrist may relieve an unhealthy mental state by recommending termination of pregnancy. On the other hand, the termination of pregnancy may later produce a severe depression with suicidal risk.

Psychiatric decision as to interruption of pregnancy is most generally required in the second month when the patient's apprehensions are at their maximum.

In contrast, psychoses associated with pregnancy usually occur in the last month of gestation or the first month of the puerperium. If a florid mental illness occurs in the mid-months of pregnancy, it is likely to be schizophrenia and to carry a poor prognosis. Decision is heavily weighted in favor of termination in such a case.

In the early months of pregnancy, psychiatric disturbances may be divided into 3 groups: (1) psychosomatic, (2) personality disturbance, and (3) social difficulties. The psychosomatic disturbances include vomiting, chorea and asthma. These can usually be carried, but termination is occasionally required. Subsequent psychiatric treatment may offer a chance for a later successful pregnancy.

Among the personality disturbances, the nature of the past illness will weight the final decision. If the past illness was a depression or elation, the pregnancy might be allowed to go to term. Where a schizophrenic illness is concerned, termination would be advised, with sterilization.

Anxiety states and hysterical reactions do not ordinarily require abortion. Rape, or forced intercourse, may be associated with social circumstances which are mentally intolerable to the patient. If a certified mental defective becomes pregnant, abortion may be justified.

A patient strained to the limit of her mental endurance by quickly repeated pregnancies sustained in an impoverished setting, may require abortion and sterilization.

Each case must be decided in respect to a very individual pattern of response with all possible facts available.

SOME CONSIDERATIONS GOVERNING THE TERMINATION OF PREGNANCY IN NEPHRITIS AND DIABETES

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Univ. Toronto M. J., 26: 226, 1949

The care of the infant, apart from breast feeding, imposes an added strain of several hundred calories per day on the metabolism of the mother with nephritis or diabetes. This increased metabolic load must be carefully weighed in the individual case.

Diabetes is inherited as a Mendelian recessive characteristic. Twenty-five per cent of the population are carriers and all children of diabetics are carriers.

Both diabetics and nephritics tend to be afflicted by arteriosclerosis, which impairs the remote prognosis of the mother. The possibility that the mother may not live to bring up the family deserves much consideration.

Acute glomerular nephritis early in pregnancy may be treated with conservatism, because it tends to improve spontaneously. A delayed resolution of the

nephritis, or acute nephritis in the later months of pregnancy, complicated by toxemia, would justify termination of gestation. In sub-acute progressive hemorrhagic nephritis, the renal injury alone would necessitate immediate interruption. On the other hand, the patient with quiescent chronic nephritis may carry through a pregnancy with little further damage. If renal insufficiency or toxemia develops, interruption may be justified. In cases of malignant arteriolosclerosis, renal insufficiency indicates termination of pregnancy.

Pregnancy in a true diabetic may exert no unfavorable influence on the disease. However, the carbohydrate tolerance of diabetic patients is usually diminished, particularly in the more severe cases. The overall maternal mortality in diabetes is 6-9 times that of non-diabetic mothers, and toxemia of pregnancy is much more common. Fetal defects, stillbirth, and abortion are likewise encountered much more often. If, at any stage, despite care, the maternal risk becomes too great, or if adequate care cannot be accomplished, termination of pregnancy is required. Because of the high proportion of deaths in utero near term, and consequent damage to both mother and fetus, cesarean section 3 weeks before term is the method of choice for delivery.

MISCELLANEOUS

STREPTOMYCIN AND PENICILLIN IN FEBRILE OBSTETRIC AND GYNECOLOGIC CONDITIONS

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Illinois M. J., 95: 156-159, March, 1949

Streptomycin and penicillin are extremely valuable therapeutic aids in obstetrics and gynecology. In 51 cases, penicillin, 25,000 U. every 3 hours, was started after 24 hours of labor when delivery was not imminent or after Dührssen's incision, intrauterine pack or like procedures were instituted. The incidence of febrile puerperium in these cases was 17.7 per cent. A control group, from 1934-35, in whom no penicillin or other agent to prevent infection was used, had an incidence of 34.3 per cent febrile puerperium. Streptomycin, in doses of 0.3 gram every 3 hours, was used in 42 cases under the same trial conditions, with an incidence of 9.5 per cent febrile puerperium.

Penicillin in doses of 50,000 U. every 3 hours 8 times daily has reduced the incidence of suppurative mastitis when treatment is instituted within 12 to 24 hours from the first symptom. When suppuration has occurred or is inevitable, penicillin is still valuable in localizing the abscess and in aiding the healing process.

Penicillin and streptomycin have been valuable in infected abortions.

It should be emphasized that streptomycin is contraindicated in urinary tract infections, except under the most pressing circumstances. Penicillin will not necessarily prevent a pyelitis or *B. coli* bacteremia.

The antibiotics do not extend obstetric and gynecologic conditions for major surgery beyond the present accepted standards.

Sufficient amounts of streptomycin and penicillin must be given and given over an appropriate period of time. The parenteral route is the only acceptable one in obstetric and gynecologic complications. Other therapies must also be employed (blood transfusions, fluids, relief of bowel distention, drainage of abscesses and other routines). Even though many smaller hospitals are not equipped to do complete diagnostic bacteriology, every effort should be made to determine the offending organism, and frequently the degree of susceptibility to penicillin and streptomycin should be established as a guide for therapy. The author presents a table of the therapeutic values of the 2 drugs for various organisms and conditions from the point of view of obstetrics and gynecology.

Gynecology

ENDOCRINOLOGY

A SURVEY OF FUNCTIONAL UTERINE BLEEDING WITH SPECIAL REFERENCE TO PROGESTERONE THERAPY

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Am. J. Obst. & Gynec. 57: 854, 1949

It has been recognized that the endometrial pattern of functional uterine bleeding is not uniform; the response to therapy might also vary, depending upon the associated endometrial pattern. The authors analyzed the cases of functional uterine bleeding seen in the gynecologic out-patient department to determine the relationship between the endometrial pattern and the response to therapy.

During the past 7 years, approximately 700 cases of functional bleeding have been seen in the out-patient department; during this period, 104 patients with severe symptoms have been selected for referral to the special functional bleeding clinic. All patients were subjected to an initial curettage. Only if abnormal bleeding recurred, was a case referred to the special clinic.

Of the 104 cases of functional bleeding, only 91 (69%) were thought suitable for endocrine therapy. An initial dose of 30 mg. of pregnenolone a day was given orally for 7 days. Twenty-eight days after the first progesterone therapy, a second course of 7 days was begun, using the same dosage. The third therapeutic cycle was given for from 5 to 7 days, 21 days after the onset of bleeding following the second course of therapy. Attempts were made to evaluate the etiological factors underlying the condition. Following the first 2 months of cyclic progesterone, some form of adjunctive therapy, consisting of diet or thyroid, was begun as indicated.

A total of 235 curettages were performed on 104 patients. The initial diagnosis was hyperplasia in 66%, interval nonsecretory in 16%, secretory in 12%, and other patterns in 6%. Thirty-seven per cent of the cases showed no change in diagnosis on subsequent curettages. Of the patients who showed a variation in pattern, none of the untreated patients showed a variation from the nonsecretory type to secretory endometrium.

Sixty-nine of the special clinic patients showed endometrial hyperplasia at the initial curettage. Fifty-six of the 69 cases were considered suitable for progesterone therapy; in this group there were no therapeutic failures. The establishment of regular menses while on therapy was the criteria of success. These women were parous and in the older age group. Of the 56 successfully treated cases, 45% had no recurrence of symptoms after the first 3-month course of progesterone therapy.

Seventeen cases, or 16%, showed interval nonsecretory endometrium on the initial curettage. Fifteen patients were judged suitable for progesterogen therapy. Thirteen had excellent results, 5 had no recurrence. Two patients failed to respond to therapy; one had pelvic inflammatory disease, the other had an ovarian neoplasm.

Three patients showed chronic endometritis. Only one patient received hormone therapy. She received 2 courses of progesterogen therapy, and had a recurrence of symptoms 6 months after cessation of her primary therapy. Two years later she was asymptomatic.

Two cases of atrophic endometrium were studied. Both were treated successfully by giving from 1 to 3 mg. of stilbestrol a day for 17 days, followed by a 7-day course of from 5 to 10 mg. of progesterone intramuscularly.

Among those referred to the special clinic were 13 patients who showed secretory endometrium. Six of the 13 patients were treated unsuccessfully with progesterone.

There were no failures of progesterogen therapy among the patients bleeding from a nonsecretory type of endometrium. Not one case of secretory endometrial bleeding has been successfully treated by progesterone. In using progesterogen therapy, 2 things should be emphasized: (1) bleeding does not cease until a week after progesterone withdrawal, and (2) it probably does not cure the underlying conditions, but only relieves the symptoms. In the series, 57% of the cases successfully treated had a return of symptoms within 6 months to 2 years after cessation of therapy. The patients who had no recurrence of symptoms had no adjunctive therapy. The fact that 18% of all cases treated became pregnant, is a strong argument for perseverance with conservative therapy of functional bleeding.

(The good results reported in this painstaking study would certainly seem to recommend a trial of the outlined plan of treatment in these frequent and troublesome cases. As the authors state, and as is true of practically all the plans of hormonal treatment of functional bleeding, this method of progesterone therapy is meant primarily to control the bleeding and not to cure the underlying cause. The latter has its site in the pituitary, and in the great majority of cases the fundamental disorder represents an aberration of the anovulatory type of cycle. It is in this group that one finds a purely proliferative and often hyperplastic endometrium, as reported by the authors in much the largest proportion of their cases. In a special study clinic like theirs curettage was done routinely before beginning treatment. In private practice one would not wish to insist on this in cases of more moderate degree in the pubertal and adolescent group, and in these not many mistakes would be made by assuming that they are of the common anovulatory type.)

Progesterone has been used by one method or another for many years in the treatment of functional bleeding and I do not believe that many would claim that the results have been brilliant, or that they have been any better than can be obtained, for example, by the estrogen plan. The latter also is meant for control rather than cure, although some have maintained, rather naively I believe, that cyclic therapy with both estrogen and progesterone will often beat the pituitary into a sort of cyclic submission. As a part of such treatment, progesterone has seemed to me to have produced unimpressive results. For mere control until the hoped for readjustment takes place, as it is likely to do sooner or later through the inauguration of ovulation, the administration of rather large doses of estrogen, usually in the form of stilbestrol, for periods of about 3 weeks, often controls and spaces the bleeding phases quite satisfactorily.

In the plan employed by others, including the authors, advantage is taken of the "medical curettage" which can apparently be brought about through comparatively moderate oral progesterone therapy. Their results in this group have been better than those reported by most others. While still other methods of endocrine therapy for functional bleeding might be discussed, my own feeling at present is that, for control of this bleeding, the two most frequently successful plans are with estrogens or with progesterone, according to some such program as that outlined by the authors.

It is possible that sooner or later some fairly precise method may be revealed of making the non-ovulating woman ovulate, in which case the largest number of functional bleeding cases should be curable. Until then, we must treat such cases on the ovarian rather than the pituitary level, and aim at control rather than cure, in the hope that spontaneous endocrine readjustment will sooner or later cure the patient, as it usually does. In discussing this subject at a recent meeting of one of our national societies, I took the liberty of harking back to the great but humble Ambroise Paré, who so often appended to his case reports the remark that "I treated the patient, but God cured him." We all treat our functional bleeding cases, but it is usually God who cures them.—Ed.)

SEX HORMONE SECRETION BY TUMORS OF THE ADRENAL CORTEX OF MICE

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Cancer Res., 9: 257, 1949

This report presents the results of a comparative study on the secretory activity of adrenal cortical tumors arising in the Bagg albino, NH, CBA, C3H, and Strong A strains of mice. These strains were suitable for such study because tumors of the adrenal cortex may be induced in them by castration. In the NH stock, such tumors occur spontaneously, particularly in females.

Tumors of the adrenal cortex of castrated male Bagg albino mice secreted androgenic hormone. Similar spontaneous tumors were present in non-castrate males of this stock 2 years of age.

The tumors induced by castration in Bagg albino female mice produced either estrogen or androgen. Extensive cortical hyperplasia and/or adenomas appeared in the intact females 2 years of age.

Secretion of androgen by cortical tumors may be a strain-limited character. It did not appear in castrated NH males or females. In the CBA and C3H stocks, cortical tumors of castrated females exhibited mixed secretory activities. Castrated Strong A female mice bearing cortical adenomas had masculinized submaxillary glands and atrophic reproductive tracts.

The histology of the submaxillary gland of the mouse is a sensitive index of androgenic secretion. Progesterone and estrogen do not duplicate the androgen effect, nor will they alter the structure of the submaxillary gland of the castrate mouse.

Ceroid pigment deposits are associated with the genesis of tumors of the adrenal cortex, testis, and ovary of mice.

UTERO-TUBAL PERSUFFLATION CURVE IN MYXEDEMA.
EFFECT OF THYROID THERAPY

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J. Clin. Endocrinol., 9: 285, 1949.

Kymographic persufflation curves were obtained during the post-menstrual period in 7 myxedematous women before and after treatment with desiccated thyroid. The utero-tubal kymographic persufflation technic described by Rubin (J. A. M. A. 90: 99, 1928), was used. In the normal woman of childbearing age, the height of the curve is 6 or 7 cm., the frequency of oscillations is 4 or 5 per minute, and the amplitude is 10 to 12 mm. It was found that the persufflation curves of the uterus and tubes in myxedematous women may be diminished in height or have oscillations which are of smaller frequency and amplitude than those of normal subjects. Thyroid therapy produces normalization of the utero-tubal persufflation curve, coincidentally with clinical improvement and increased basal metabolism.

Rubin considered the oscillations to be due to contractions of the tubes. Stabile considered the oscillations to be due to variations in the resistance of the uterus and tubes to the passage of gas; the resistance is directly related to the tone of the uterine and tubal muscle. Whichever explanation is admitted the oscillations are evidently of muscular origin. In myxedematous patients, anatomic and functional changes take place in various organs containing muscular tissue: dilatation of the heart, megacolon, dolicoecolon, megaduodenum, and atony of the bladder have been described. All these disorders disappear with the administration of desiccated thyroid.

(This is an interesting study, though the series is too small to be of much statistical value. The results reported are perhaps not very surprising in view of the known constitutional manifestations of hypothyroidism. They may help to explain the good results which most clinicians accept as accruing from thyroid therapy in cases of sterility, especially when there is definite clinical and laboratory evidence of thyroid deficiency. These good results quite certainly are not limited to the effect upon the tubal musculature, but unfortunately the other and probably more important benefits which many assume for thyroid therapy, including even an effect on the gonads or on the quality of the germ plasma, can not be as tangibly and objectively studied as can the effects upon the muscular function of the tube.—Ed.)

THE EFFECT OF ENDOCRINES ON FIBRO-ADENOSIS

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Brit. M. J., 1: 750, 1949

Fibro-adenosis may be defined as a painful or nodular condition of the breast not due to new growth, bacterial inflammation, or fat necrosis. The author investigated the effect of estrogens and androgens on the disease. In nearly every case a sample of breast tissue was taken by biopsy before treatment. A second sample was taken at the conclusion of treatment and at a corresponding period in the menstrual cycle.

Thirty-three cases were given at least 80 mg. of estradiol benzoate by injection in 4 weeks or 280 mg. of stilbestrol by mouth in 8 weeks. Estrogens were harmful if given in doses large enough to be effective. Histologically the fibroblastic reaction, the epitheliosis, and the adenosis tended to increase.

Thirty-four patients received injections of testosterone propionate; 22 had at least 400 mg. in 4 weeks. It was found that the majority of the patients benefited temporarily by these injections. Eight of these patients suffered hirsuties, amenorrhea, and deepening of the voice. It was concluded that the risks entailed in this form of therapy did not justify the temporary relief obtained.

Twelve patients received 15 mg. of methyl testosterone by mouth daily for 2 months. Seven were relieved of their symptoms for an average of 7 months; one was relieved only while taking the tablets; three had no relief of their symptoms.

Nineteen patients received 400 mg. of testosterone propionate in the form of "neo-hombreol" ointment for a period of one month. Six of these patients were relieved for an average period of $4\frac{1}{2}$ months.

Eleven patients received 100 mg. of testosterone implanted deep into the breast tissue at the time of the first biopsy. Four were relieved of symptoms for 1, 2, 3, and 6 months, followed by a relapse.

In a substantial proportion of cases, androgen therapy causes temporary improvement in the symptoms of fibroadenosis. The safest, most effective and most convenient way of administration is in doses of 15 mg. of methyl testosterone by mouth daily for 2 months. Androgen therapy has no constant detectable effect on the histological picture.

(The fibro-adenosis studied by the author represents at least one type of the so-called chronic mastitis or chronic cystic mastitis which is so often encountered by gynecologists in their daily work. In many cases the only complaint is pain and tenderness at the menstrual periods, and sometimes intermenstrually as well, but with breasts which are normal on palpation. Cases of this sort are best designated as mastodynia. In others, however, there is marked duct thickening, sometimes rather uneven and nodular, with often innumerable tiny cysts which produce the so-called "shotty" breast. Often larger cysts are found, sometimes multiple, and not infrequently these are transitory. It is not rare to find that even rather large cysts appear, or disappear, almost over night, but others are persistent, and may if they are large cause some pain and tenderness, not to speak of the cancerophobia

which is almost an inevitable accompaniment of any breast condition these days, whether the manifestations are objective ones or purely subjective.

The gynecologist should be fully familiar with the various forms and degrees of this endocrine-induced breast condition, but above all he must be able to distinguish them from lesions which are suspicious of cancer or obviously malignant. He must be pretty sure of his ground if he assures his patient, as he can often conscientiously do, that the pain and tenderness, or the multiple small cysts, or the diffuse duct thickening represents only the reaction of certain breast tissues to the stimulus of the ovarian hormones. If he has the slightest doubt about the innocence of the breast condition, and in at least some lesions which he feels sure are benign, the proper treatment is surgical, usually involving biopsy and immediate microscopic examination, but it would lead us too far afield to discuss all the possible ramifications of this subject.

Although the fibro-adenosis which the author describes undoubtedly represents an endocrine breast response, I do not believe that endocrine therapy is often necessary, and I feel that it is wise to avoid it if possible. Not only is such therapy of questionable value, but it is temporary and it keeps the patient's mind centered on her trouble.

My own experience has been that if the physician, after careful examination, is convinced of the innocuousness of the breast condition, and if he can put this over forcefully to the patient, with a simple explanation of why she has her breast symptoms, the latter will at once be improved. Once she knows that the symptoms have nothing to do with cancer, her mind is relieved because the psychogenic accentuation of her breast soreness and twinges is abolished. Proper support of the breast and the occasional use of an ice bag may be helpful in more persistent cases, but only rarely endocrine therapy.

Estrogen therapy, and in latter years especially stilbestrol, has been used by many in such cases, but with what seems to me a complete lack of rationale. General surgeons have been especially culpable in this respect. I recall that many of them, including some very distinguished leaders, used to recommend the "ovarian residue" or the ovarian tablets which, before we had the pure hormone principles, constituted the ovarian therapy of the day. Aside from the illogicalness of such therapy, we can be sure, in retrospect, that it was worthless. Equally illogical would seem to be the use for this indication of the potent oral or hypodermic estrogen preparations now available, and, since the estrogens are responsible for the symptoms, such therapy might be expected to worsen the latter.

Testosterone, which in some respects is anti-estrogenic, would seem to be the logical agent to employ in the few cases in which any hormone at all seems necessary, and the studies of Atkins appear to bear out this idea. I still feel, however, that endocrine therapy should be avoided when possible, and that in the vast majority of cases such simple measures as proper support of the breast, combined with reassurance and psychotherapy, are all that the patient needs.—Ed.)

DEVELOPMENT OF LEIOMYOMAS IN FEMALE RATS WITH AN ENDOCRINE IMBALANCE

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Cancer Res., 9: 277, 1949

Smooth muscle tumors of the uterus are rare in rats. Prior to the present observation, they had never been seen in a Yale rat colony.

One hundred eighty-five newborn female rats received testis grafts in the neck. Sixteen of these rats survived over 3 years. An endocrine imbalance is usually established in female rats with testis transplants by the time they reach sexual maturity. This fact is expressed by the presence of constant estrus. Pyometra is usually observed in these animals beginning after 6 months of age. Among the 16 rats which survived more than 3 years, 4 had leiomyomas of the uterus. One had multiple tumors; 2 were located in the middle and lower third of the right cornu, and a third was near the cervical end of the left cornu. The other three animals had single tumors. In one of these, the tumor was located in the right cornu; in the other 2, it was in the left cornu.

The tumors in the rats' uteri described here are similar in all respects to the fibromyomas which occur so frequently in the human female. On the other hand, leiomyomas are extremely rare in rats. None of the rats in this study had become pregnant. The endocrine imbalance in these rats keeps the uterus under the influence of a chronic low level of estrogen which allows pyometra to develop, due to the continuous exposure of the uterus to the bacterial flora of the vagina. It is felt that when the animals are able to survive the pyometra until old age, the chronic stimulation of the smooth muscle by the estrogen greatly enhances the chances of tumor formation. Multiple leiomyomas have not been previously described in the rat.

(The etiology of uterine myoma is still unknown but the hypothesis of endocrine responsibility has been put forth by many authors. I have always felt that the evidence for this was very flimsy. The fact that myomas characteristically regress after the menopause would seem better explainable by the fact that the blood supply of the tumors is greatly lessened, so that the tumors, as well as the uterus and vagina, might well be expected to undergo retrogression. The ovarian estrogen might be looked upon as necessary to the continued growth of the tumors, but this does not indicate that the origin of the neoplasms is to be attributed to the hormones.

So far as I know, it has not been possible heretofore, with one possible exception, to bring about uterine myoma formation by long-continued estrogen administration in experimental animals. In only one instance, that reported by Nelson many years ago, was a myoma found in one of a series of monkeys thus treated, and it would be difficult to eliminate the possibility of spontaneous occurrence in this one case. It is true that tiny nodules can be produced in the subperitoneal fibrous tissue by prolonged estrogen administration, but histologically these are fibromas and not myomas. Their structure resembles that of the fibromas produced by similar estrogen administration in guinea pigs. The remarkable fibromatogenesis produced in this particular species by Lipschütz and his co-workers has often been wrongly adduced in support of the endocrine etiology of myomas. The fibromas of Lipschütz, however, aside from their complete lack of histological resemblance to myomas, occur, not in the wall of the uterus, but in the subperitoneal layer, and far more frequently and in much larger size in any of the connective tissues of the pelvis or general abdominal cavity. Furthermore, they are not real tumors, as they disappear after cessation of the estrogen, or after treatment with progesterone. As a matter of fact, they do not develop if progesterone and estrogen are administered together.

Pfeiffer's experiments, therefore, constitute a real contribution to this question, and would seem to furnish more substantial evidence than has hitherto been available for the role of the estrogens in the incitation of myoma development. Whether or not the rather unique way in which the author brought about the endocrine imbalance plays any important role in yielding the positive results, I do not know. In any event, the animals are re-

ported to have shown continued estrus, so that it is logical to assume that it is the factor of continued estrogen stimulation which is the important one. It is to be hoped that the author, as well as others, will pursue this line of investigation, so that more light may be thrown upon a hitherto hazy subject.—Ed.)

THE EFFECTS OF PROLONGED THERAPY WITH DIETHYLSTILBESTROL UPON THE ENDOMETRIUM

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Lahey Clin. Bull., 6: 80, 1949

The authors report the results of endometrial biopsies performed after 18 and 24 months' therapy with diethylstilbestrol in 2 cases of endometriosis.

The first patient was given 3 mg. diethylstilbestrol daily for 6 months; the dosage was then increased to 5 mg. daily and maintained at this level. After one year of therapy, an endometrial biopsy revealed hyperplasia of the endometrium without any malignant changes. After 2 years of therapy, biopsy revealed a hypoplastic endometrium.

The second patient was given 3 mg. diethylstilbestrol for 18 months. An endometrial biopsy showed findings consistent with those of a hypoplastic endometrium.

(There is nothing paradoxical about the fact that these experiments with long continued dosage with diethylstilbestrol should under some conditions yield hyperplasia and in others hypoplasia of the endometrium. There is no doubt that the immediate effect of a strong estrogen stimulation of the endometrium is to produce hyperplastic changes. But one must reckon not only with the direct effect upon the endometrium but also the effect upon the pituitary and ovary. It is well established that excessive and prolonged estrogen administration inhibits the pituitary gonadotrophes, and thereby the ovarian production of estrogens. For example, the ovary can be converted into a functionless organ by giving sufficient estrogen, though it tends to bounce back fairly soon after cessation of the therapy. Just how the endometrium will react is probably a summation of the direct and indirect effects of overdosage with estrogen, and it is probable that the quantitative factors involved will show wide variations, just as there are wide individual variations in the sensitivity or refractoriness of different endometria.—Ed.)

THE MENSTRUAL CYCLE

ESSENTIAL DYSMENORRHEA—ITS PATHOGENESIS AND TREATMENT

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Ohio M. J., 45: 358, 1949

Pain occurs where ischemic muscle contracts. Uterine muscle contraction is believed to be under ovarian hormonal control. Knaus, E. Novak and Reynolds, and Falls believe that estrogen increases uterine contractions and that progesterin nullifies this action.

J. Novak and Harnik believe that all cases of essential dysmenorrhea are explained on the basis of psychic trauma. Davis and Cotte believe that a neuritis of the pre-sacral plexus is an important cause of essential dysmenorrhea. Wilson and Kurzrok observed that only patients who ovulated can have essential dysmenorrhea. The hormonal mechanism of essential dysmenorrhea is due to the action of estrogen and progesterin. Estrogen is thought to be a vasodilator, a diuretic, and an excretor of sodium chloride. This action is due to the liberation of acetylcholine and to the inhibition of the pituitary gland. Progesterin, formed after ovulation, tends to nullify this action of estrogen. Dysmenorrhea is often associated with hypothyroidism; there is increased pituitary activity, causing an increase in vasospasm and retention of water and sodium chloride.

Treatment of essential dysmenorrhea may include the following: (1) psychiatric consultation, (2) salt-poor diet, ammonium chloride and forcing of fluids in the latter half of the cycle, (3) use of thyroid when indicated, (4) use of vasodilators, (5) use of estrogens to establish an anovulatory cycle, (6) prolonged dilatation of the cervix, causing an overstretching of the sensory corpuscles of Kieffer, and (7) pre-sacral neurectomy.

(The cause of primary dysmenorrhea still remains an enigma. In former years the factors chiefly discussed were the constitutional, the psychogenic and the obstructive. The latter explanation has been pretty generally abandoned, but the first two factors are still to be reckoned with as of importance in many cases. While I certainly do not believe that the psychogenic factor explains all cases, as do some gynecologists, it probably is the important one in some and it can never be lost sight of in the management of dysmenorrhea patients.)

With the discovery of the endocrine control of uterine contractility, it was natural to turn to the endocrines for an explanation of primary menstrual pain. Estrogen was shown to be, as still seems unquestionably true, the hormone responsible for the contractility of uterine muscle, and for a time the consensus among investigators, based to a large extent on the investigations of Knaus, was that progesterone was the normal inhibitor of such contractility. This would be what one might expect from a teleological standpoint, as it would seem to be desirable that the uterus be put at rest or splinted in order not to interfere with nidation. However purposeful such an effect might seem to be, the work of Wilson and Kurzrok, as well as many others, has thrown serious doubt on the correctness of this con-

ported to have shown continued estrus, so that it is logical to assume that it is the factor of continued estrogen stimulation which is the important one. It is to be hoped that the author, as well as others, will pursue this line of investigation, so that more light may be thrown upon a hitherto hazy subject.—Ed.)

THE EFFECTS OF PROLONGED THERAPY WITH DIETHYLSTILBESTROL UPON THE ENDOMETRIUM

LEWIS M. HURXTHAL AND W. T. ARNOLD

Lahey Clin. Bull., 6: 80, 1949

The authors report the results of endometrial biopsies performed after 18 and 24 months' therapy with diethylstilbestrol in 2 cases of endometriosis.

The first patient was given 3 mg. diethylstilbestrol daily for 6 months; the dosage was then increased to 5 mg. daily and maintained at this level. After one year of therapy, an endometrial biopsy revealed hyperplasia of the endometrium without any malignant changes. After 2 years of therapy, biopsy revealed a hypoplastic endometrium.

The second patient was given 3 mg. diethylstilbestrol for 18 months. An endometrial biopsy showed findings consistent with those of a hypoplastic endometrium.

(There is nothing paradoxical about the fact that these experiments with long continued dosage with diethylstilbestrol should under some conditions yield hyperplasia and in others hypoplasia of the endometrium. There is no doubt that the immediate effect of a strong estrogen stimulation of the endometrium is to produce hyperplastic changes. But one must reckon not only with the direct effect upon the endometrium but also the effect upon the pituitary and ovary. It is well established that excessive and prolonged estrogen administration inhibits the pituitary gonadotrophes, and thereby the ovarian production of estrogens. For example, the ovary can be converted into a functionless organ by giving sufficient estrogen, though it tends to bounce back fairly soon after cessation of the therapy. Just how the endometrium will react is probably a summation of the direct and indirect effects of overdosage with estrogen, and it is probable that the quantitative factors involved will show wide variations, just as there are wide individual variations in the sensitivity or refractoriness of different endometria.—Ed.)

abolished. As a matter of fact, I personally more frequently employ presacral sympathectomy in this secondary or combined fashion than I do as a primary procedure in patients with entirely normal organs.—Ed.)

PHYSIOLOGY OF THE MENOPAUSE

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Am. Practitioner, 3: 481, 1949

The menopause is that era when the menstrual cycle and the reproductive function terminate. It is an aspect of aging, it has multiple psychosomatic manifestations, and recently it has been the subject of considerable endocrine investigation.

The primary alteration is in the ovary. Ovulation and luteinization disappear; thereafter, the endometrium atrophies, the ovarian cortex shrinks and the quantity of estrogen excreted diminishes and finally disappears. The basophilic cells and the acidophilic cells of the anterior pituitary show a high state of activity. Co-existent with these anatomic variations is a tremendous increase in the quantity of gonadotropin in the blood and urine. The uterus becomes smaller, the vaginal mucosa loses its cornified epithelium, and the genital organs lose their muscle tone and fascial strength.

The fifth decade is the age of the natural menopause. Menstruation disappears gradually, tapering off both in amount and time. A final cessation of the catamenia takes place in about 3 years. In a small minority, the periods cease abruptly. The aging ovary first loses its luteinizing function and acquires a mild degree of follicular hyperplasia. Abnormal uterine bleeding may then occur owing to the prolonged production of estrogen. As a group, such women have relatively few vasomotor symptoms, presumably because sufficient estrogen circulates to prevent their appearance.

Seventy-five per cent of women suffer more or less from menopausal symptoms. Only about 10% are incapacitated. Apart from abnormal bleeding, the component symptoms of the menopausal syndrome are entirely subjective. The most common of these is the so-called hot flush—a sudden sensation of heat in the upper part of the body, frequently followed by perspiration and occasionally terminated by chilliness. Lack of energy, irritability and insomnia are other symptoms. Occasionally easy fatigability is marked. Psychic manifestations, principally anxiety, are not of pathological intensity. A recurring fear of pregnancy due to the amenorrhea, may also complicate the emotional picture.

To make certain that the menopause is not the sole cause of the patient's complaints, a thorough evaluation of the patient is necessary. Most women do not require specific treatment. The elimination of numerous legendary misconcep-

cept of the inhibiting effect of progesterone. As a matter of fact we cannot be sure that heightened uterine contractility has anything to do with the etiology of dysmenorrhea, in spite of the fact that such a factor is suggested by the characteristically colicky nature of the menstrual pain in most cases. In the past few years there has been a tendency to invoke the spiral arteriolar apparatus as the seat of the disorder, but certainly this viewpoint has not been clearly established.

It has always seemed strange to me that in the common type of anovulatory functional bleeding there is characteristically no complaint of menstrual pain, though the uterine musculature is under the influence of estrogen alone, with no progesterone. On the other hand, it is the women who ovulate normally and whose ovaries produce both estrogen and progesterone who are prone to have primary dysmenorrhea. As a matter of fact, the existence of a typical primary dysmenorrhea may, I believe, be considered *prima facie* evidence that the patient is ovulating. Such observations as these are difficult to reconcile with the muscle theory of causation and for that matter, even with the vascular theory. If a satisfactory explanation of these apparently paradoxical observations could be given, I believe that this age-old riddle of primary dysmenorrhea would be pretty close to solution.

As for the treatment of this disorder, I confess that I have in recent years become less and less enthusiastic as to the effectiveness of the hormone plans which have in the past enjoyed considerable vogue, progesterone and testosterone being the hormones most often employed. On the other hand, I believe that estrogen therapy is of frequent though perhaps limited value. The virtue of estrogen treatment is that, when properly used, it can inhibit ovulation for the particular cycle and, as already stated, an anovulatory cycle is quite sure to be a painless one. To convert an ovulatory to an anovulatory cycle, estrogen in moderately large dosage is begun very early in the cycle, usually on about the second day of menstruation, and kept up for about 2 weeks. For the first series, in order to ensure the result as much as possible, a 1 mg. tablet of stilbestrol is given nightly. If for any reason the stilbestrol cannot be tolerated, corresponding doses of one of the other oral estrogens may be substituted. Almost always the succeeding menstruation is painless or nearly so, and the patient is surprised to find that she can menstruate without pain. This gives her a great psychological lift, and one can never minimize the importance of the psychologic factor in these cases. A repetition of the stilbestrol therapy with the following cycle, perhaps in 1/2 mg. doses, may again give considerable relief, though usually less striking. There are certain disadvantages of this treatment, such as the fact that the menstrual tempo is likely to be disturbed, and the patient should be prepared for this. Again, in young married women anxious for children, inhibition of ovulation is not desirable except in very intermittent fashion. But even when used intermittently, as it should be, the estrogen plan is a worthwhile addition to our not too heavily stocked armamentarium in the management of these cases. In probably the largest number of cases of primary dysmenorrhea, the pain is of short duration, often limited to the first day of the period. In most cases of this sort, I personally would prefer to abjure any form of endocrine therapy and be content with making the girls' discomfort as tolerable as possible with adequate dosage of such analgesics as codeine and aspirin. I need scarcely say that in every case full advantage should be also taken of all possible constitutional and psychotherapeutic measures.

Finally, in the severe and intractable cases, the operation of presacral neurectomy is fully justified, and it may be expected to give relief in something like 70 per cent of the cases, though some authors put the figure considerably higher. The operation, however, is an abdominal one and it must be properly done to get the best results. One would not wish to advise it too lightly, or to resort to it if the patient can get along reasonably well with simpler plans of treatment, as is most often the case. The indication for presacral neurectomy is definitely greater in cases where there is question as to the primary or essential nature of the dysmenorrhea, as when there is a very sharp retroflexion or a strong probability of endometriosis. The combination of presacral neurectomy with other corrective procedures is always advisable to make as nearly certain as possible that the menstrual pain will be

VULVA AND VAGINA

THE VAGINA IN RECONSTRUCTIVE SURGERY: A HISTOLOGIC STUDY OF ITS STRUCTURAL COMPONENTS

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Am. J. Surg., 77: 547, 1949

A review of the literature dealing with the histologic structure of the vaginal wall reveals a multitude of contradictory views. The present study was based on the microscopy of 14 specimens, each consisting of the entire vagina from the vesicovaginal junction to and including the anoperineal body and the fused urethrovaginal wall. Of these specimens, 6 were removed from the cadavers of fetuses and infants; the remaining specimens were removed from adult cadavers. Only cadavers presenting no pelvic disease were selected.

The vaginal wall can be divided into 3 layers: the epithelium, the substantia propria and the musculo-fibro-elastic layer. The vaginal wall lacks glands and lymphatic tissue. The rugae are large and prominent in the fetus and infant; they tend to become flattened in adult life and are almost obliterated in the senile period.

The epithelium is similar in all ages. The substantia propria is similar in architectural pattern at all ages and is free of intrinsic muscle fibers. The musculo-fibro-elastic layer is fused anteriorly with the urethra and posteriorly with the anoperineal body. The musculature of this layer is involuntary in type and relatively scant. There is no definite arrangement into a circular and a longitudinal layer.

The elastic tissue layer is the most important component of the vaginal wall. It is more compact and abundant at the base of the cardinal ligament; it follows the blood vessels as they approach the cervico-vaginal area. As the elastica descends into the vagina, it diffuses and intermingles with the fibrous tissue and muscle fiber elements and also forms a peripheral vaginal wall band.

There is no definite layer of muscle in the vagina; the few muscle fibers present are circular, oblique and longitudinal. The greatest number of muscle fibers are found in the middle third of the vagina. In the young adult the muscle is firmer; with advancing age, atrophy sets in and in the senile period there is almost complete absence of muscle fibers.

(The senior author of this paper has in recent years published a number of valuable anatomical studies of pelvic structure, especially of the pelvic fascias. The present contribution represents a continuation of this work, and it should be of interest and value to all those who do pelvic reconstructive surgery.—Ed.)

tions from the patient's mind is of value and mild sedatives may be employed. Estrogen therapy is specific if the symptoms are severe. The oral route is especially suitable, and there seems to be no need for parenteral administration of estrogens. The smallest possible dose should be employed and the estrogen should be gradually withdrawn after a limited period. On estrogen withdrawal bleeding may occur; the physician must be certain that any vaginal bleeding is not due to uterine malignancy.

Estrogen therapy is contra-indicated if menstrual irregularity has been present before the menopause, if the patient has been castrated because of endometriosis, in women of cancer families, in the presence of uterine myomas and mammary fibroadenomas, as well as in patients with a history of recent hepatitis.

(A simple, short and sensible review of the subject, which the general practitioner especially can read with profit.—Ed.)

serum-Ringer's solution with an equal part of a 1 per cent solution of an enzymatic yeast protein hydrolysate containing agar, carbohydrates, and liver extract.

By usual laboratory methods, 51 cases of trichomonad vaginitis in 58 studies were diagnosed. The use of a yeast protein hydrolysate-enriched medium permitted the remaining cases to be culturally diagnosed as positive.

CYLINDROMA OF THE VULVA: ADENOCARCINOMA, CYLINDROMA TYPE, OF THE VULVA: REPORT OF A CASE OF TWENTY-SEVEN YEARS' DURATION

GEORGE P. SAYRE

Proc. Mayo Clin., 24: 224, 1949

A 32 year old woman was first seen in 1924 complaining of a small growth on the vulva of 4 years' duration. On physical examination a small hard mass was found in the region of the left Bartholin gland. At operation the tumor was found to extend backward and involve the anal sphincter; it could not be entirely removed. The pathological diagnosis was malignant adenoma of Bartholin's gland. Postoperatively the patient received radium to the area of the tumor and to the right groin. Two years later there was no evidence of recurrence.

In 1931 a small hard nodule was noted by the patient in the region of the former wound. Wide surgical excision revealed recurrent carcinoma. The patient received lead phosphate for 2 years, a total of 918 mg. Nevertheless, adenocarcinoma persisted and from 1933 to 1936, the patient received repeated courses of radium therapy locally. In 1943 the patient returned because of acute retention of urine. The tumor was found to extend to involve the whole perineum and laterally to involve the right buttock. The urethra was dilated and radium therapy was again given. Nevertheless, the local lesion extended further. Metastases developed in the femur, in the left pubic bone and the right lung. The patient finally expired 23 years after her first admission to the hospital.

At autopsy, the lungs and liver contained numerous metastases. The perineum was replaced by enormous ulceration. There was an acute cystitis with bilateral hydroureter and hydronephrosis. There were extensive generalized skeletal metastases.

Microscopically the tumor consisted of irregular glands imbedded in dense fibrous tissue. Typically the glands consisted of broad cords of cells with 2 or more irregular lumina. Mitotic figures were very infrequent. Permeation of blood vessels was not seen. The metastatic lesions showed a similar picture. The tumor resembled biopsy specimens taken earlier in the patient's course.

The term "cylindroma" was first used by Billroth in tumors of the salivary glands to describe a lesion marked by cords or cylinders of epithelial cells surrounded by dense connective tissue columns. Ewing listed these tumors as true

THE USE OF ESTROGENIC CREAM IN THE TREATMENT OF
SENILE VAGINITIS

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Am. J. Obst. & Gynec., 57: 1018, 1949

It has been known that estrogenic hormones given by injection or orally may relieve the symptoms of vulvovaginitis, atrophic vaginitis or senile vaginitis; often the dosage must be so great that irregular or withdrawal bleeding may result. The use of an estrogen in a cream base has been reported by Rakoff (1947).

In this investigation, 123 patients received dienestrol in a cream base for the treatment of atrophic changes in the vaginal mucosa. Each patient was given 4.46 gm. of cream containing 0.446 mg. of dienestrol with instructions to use it every night. In 68.3% of the cases the vaginal mucosa appeared healthy and the patients had no complaints. Twenty-five per cent of the cases were classified as unimproved; however it was noted that the patients showed either symptomatic or clinical improvement. Relief of symptoms had to be accompanied by clinical response before the patient was considered improved. The average healthy vagina was maintained in some instances by using dienestrol one to three times a week over a period of months. No untoward effects were noted.

(Although I have had no experience with the use of estrogenic cream in the treatment of senile vaginitis, I have no doubt that it is helpful, just as is the vaginal administration of estrogen in the form of suppositories. I have always felt that for this indication the vaginal route for estrogen therapy is preferable to the oral, that a smaller dosage will suffice to bring about the desired local effect, and that bleeding is less likely to be produced. However, no method of estrogen therapy is foolproof as regards the hazard of postmenopausal bleeding, which is always a possibility if treatment is excessive or too prolonged, whether the route be oral, parenteral or vaginal.—Ed.)

A CULTURAL METHOD FOR THE DIAGNOSIS OF TRICHO-
MONAD INFESTATIONS

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Am. J. Obst. & Gynec., 57: 980, 1949

Until recently, culturing of vaginal discharges for trichomonads has been inconvenient since a practical medium adequately supporting their growth and permitting reproduction in a short period of time has not been available. Such a medium has been devised for the primary isolation of trichomonads from vaginal discharges and has been used for over one year. The medium consists of a 2:3

THE UTERUS

THE ISTHMIC MUCOUS MEMBRANE OF THE HUMAN UTERUS

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Science 109: 383, 1949

Preliminary studies have been made of the mucous membrane of 38 human uteri removed at operation. In each of these cases, similar blocks of the isthmic mucous membrane were prepared for comparison with the endometrial specimens.

Comparison of the endometrial functionalis with the isthmic mucosa indicates that the isthmic mucosa is not peculiar, but rather, it is an integral part of the corporeal endometrium. The isthmic mucosa is a continuation of the endometrial basalis and it differs from the endometrium proper only in that the functional layer is lacking.

These observations cast doubt upon the propriety of designating the isthmus uteri as an entity of equal importance with the cervix and corpus. They suggest that this zone is part of the corpus uteri.

(Readers are familiar with the outstanding contributions of the senior author of this paper to the study of the lower uterine segment, especially as to its musculature. The present paper deals with the mucous membrane of the isthmus, which in a previous generation was set aside as a separate subdivision of the uterus. The latter, in many of the descriptions of the day, was divided into the corpus, the isthmus and the cervix, and this was done chiefly on the basis of assumed differences in the lining mucosa. I recall that in a number of anatomical studies, especially from the German School, it was emphasized that in the isthmus the glands extend characteristically obliquely downward from the surface orifices toward the cervix, while those of the corpus run transversely or obliquely upward.

The present authors, I gather, made no such observation, although they did find that in the isthmus the functional lower layer is lacking. A difference does therefore seem to exist, though I agree with the authors that this would scarcely justify considering the isthmus as a separate entity.—Ed.)

SUSPENSION AND THE RETROFLEXED UTERUS. A REVIEW OF CASES

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Am. J. Obst. and Gynec. 57: 959, 1949

During the years 1925 to 1946, 93 suspensions were performed for retroflexed uteri. Questionnaires were sent to these patients and 44 replies were received.

carcinoma and emphasized that they have a long history, that they promptly recur after extirpation, and that the patient may appear to be in good health despite extensive metastases. Dockerty and Mayo showed that these tumors spread by the perineural lymphatic vessels.

Tumors of Bartholin's gland are relatively infrequent. True malignant tumors of this gland have the characteristics of adenocarcinomas elsewhere. The cylindromatous type of Bartholin gland tumor has been reported in 2 other cases. It is noted that Bartholin's gland is the female analogue of Cowper's gland. The rare tumors of the latter are also described as cylindromas.

(Without having available photomicrographs of this tumor, it is difficult to make any comment. So far as I had known, the designation of cylindroma had not previously been applied to a vulva tumor, although the author states that 2 cases of Bartholin's gland carcinoma had been considered cylindromatous. No longer is the term cylindroma applied to certain tumors of the ovary, as it once was, since we have learned that tumors formerly so-designated are now more correctly classifiable. Most of this group represent granuloma-cell tumors of the so-called cylindromatous type.

In the salivary gland there does occur a peculiar "cylindroma," made up of nests of closely packed epithelial cells but with so many small cyst-like spaces as to present almost a sieve-like picture. A good illustration of this tumor type is to be found in Ewing's "Neoplastic Diseases." It does not comport with the description by the author of "irregular glands imbedded in fibrous tissue."—Ed.)

CYTOLOGIC DIAGNOSIS OF UTERINE CANCER BY EXAMINATION
OF VAGINAL AND UTERINE SECRETIONS

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Am. J. Clin. Path., 19: 301, 1949

In spite of the progress that has been made in the use of the vaginal smear during the last few years, we have not yet reached a point where we can consider it as a method of final diagnosis. Whenever possible, confirmation of smear findings with biopsy of curetted or excised tissue is recommended.

The staining procedure is not specific for cancer cells, but only adapted to cancer diagnosis. It consists of the staining of the nucleus with Harris' Hematoxylin and counterstaining of the cytoplasm with Orange G and EA36 or EA50.

The four types of smears are (1) aspiration vaginal smear, taken before the introduction of a speculum, (2) endocervical aspiration smear, (3) cervical swab smear, and (4) endometrial aspiration smear. In cases where all four types of smears are available, the chances of missing a malignant lesion are greatly reduced. Most of the statistics available at present are based on vaginal aspiration and cervical aspiration or swab smears.

In a group of 124 patients with symptoms, the incidence of uterine cancer was relatively high, 16.1%. In a second group of patients who were asymptomatic (777 patients), the incidence of uterine cancer was 1.4%. Two of the positive cases in the first group (all proved by biopsy) had been reported by the author as negative, 10% false negatives. In the second group there was 9.1% of false negatives. There were no false positives in the first group; in the second group the percentage of false positives was 0.03%. A statistical evaluation of 3,195 cases examined at the Kate Depew Strang Cancer Prevention Clinic shows a lower incidence of uterine cancer, 0.3% as proved by biopsy. In this series there were no false negative reports and only one false positive, giving a percentage of 0.03.

The criteria used in the cytologic diagnosis of cancer are based on structural modifications of the cancer cells and of their nuclei as well as on changes in their relationship and pattern when in groups and clusters. Increased knowledge and experience are now enabling the author to recognize with greater confidence characteristic cell or smear types; in some instances, it is possible to evaluate the type of tumor.

One smear type is referred to as "superficial dyskaryosis." Smears of this type are characterized by the presence of enlarged and hyperchromatic nuclei. Binucleated or multinucleated cells are not uncommon. Some of the abnormal cells show cornification and are acidophilic. In cases exhibiting this smear type, a high incidence of early carcinoma of the cervix, of the intra-epithelial type, has been found to exist. The author considers cases of this type as suggestive of an early localized low grade malignant neoplasm of the cervix.

There were 20 cases of uncomplicated retroflexion. Only 7 cases (35%) had complete relief of all their symptoms. There was no consistency between which symptoms were relieved and which not.

There were 10 cases with cervicitis and/or erosion in which suspension and cauterization was done. Six cases had complete relief of symptoms. There was a definite lack of consistency in the relief of symptoms with the exception of back ache. In addition to suspension, trachelorrhaphy was done in 2 cases; trachelorrhaphy and perineorrhaphy in 2 cases; enucleation of fibroids in 2; curettage in 2; presacral sympathectomy in 2; repair of cystocele in 2; and oophorectomy, curettage, cauterization and presacral sympathectomy in one case. Of these 24 cases, 59% experienced complete alleviation of their symptoms. The other operations performed in addition to the suspensions were probably responsible for the cure of many of the symptoms. The results throw skepticism on the indications for suspension in uncomplicated retroflexion usually given in textbooks: habitual abortion, sterility, iliac pain, backache, and dysmenorrhea.

Suspension has not played a satisfactory part in the cure of uncomplicated retroversions. The author does not do a suspension except under these conditions: (1) the uterus is anteverted, (2) a Hodge pessary is inserted and left for 3 months, (3) the pessary is removed and left out for a month. If the symptoms are relieved as a result of the insertion of the pessary and recur when the pessary is removed, suspension might be justified.

(The follow-up studies reported by Perlin show results which fully justify the conservative attitude of modern gynecologists as regards suspension operations for retrodisplaced uteri. In many clinics of a former day, "Suspension and appendectomy" was rarely missing from the daily operating room poster; now it is conspicuously lacking in most clinics. To say that the operation is still not abused would be as inaccurate as to say that innocent cystic ovaries are no longer fair game to some surgeons, and that many normal uteri are not removed. The surgical millenium has not been reached in our specialty, or in any division of surgery. But most gynecologists now appreciate that a woman can be just as happy and healthy if she wears her uterus backwards as if it is anterior, and that backache is far more frequently due to trouble in the back itself than to the fact that "the womb is pressing on the back," as many patients quote their doctors. It would be silly to say that suspension operations have no place at all, because of course they have, in some cases of acquired but very few of the congenital type of retroflexion. In the sharply retroflexed subinvolved uterus, where the vascular congestion factor is often much more important than the mechanical one in explaining the menstrual pain or excess and the backache of which such patients complain, a properly performed hysteropexy is fully justified after preliminary study, often with the use of pessaries, as recommended by the author, to demonstrate the responsibility of the displacement in the production of the symptoms. In many cases of this group, the cervix has swung downward and forward along the vaginal axis, with the marked elongation of the uterosacral ligaments which alone permits the cervix thus to swing away from its posterior mooring. Under these circumstances a suspension operation is quite likely to prove unsuccessful unless it is combined with a plicating shortening of the uterosacral ligaments. Again, some form of suspension is clearly indicated in those conservative operations in which the conserved uterus presents a raw or oozing posterior surface which otherwise would ensure its matting to the rectum. Nor do these represent the only proper indications for suspension. It is the frequent abuse rather than the not infrequent proper use of the suspension operation which needs emphasis.—Ed.)

Nine cases were reported in some detail to illustrate the diagnosis of genital carcinoma by the vaginal smear method. These 9 cases included 5 squamous cell carcinomas of the cervix, one squamous cell carcinoma of the vulva, one sarcoma of the uterus, one chorionepithelioma and one primary carcinoma of the oviduct in which the tumor mass was 3 cm. from the uterine cavity. Those patients having squamous cell carcinoma of the cervix showed that sometimes the diagnosis of malignancy may be made earlier by smears than by the biopsy method. One patient with adenocarcinoma of the endometrium in which smears were negative even when they were obtained from the tumor was also reported to show one of the weaknesses of the smear method.

The authors have briefly reviewed the advantages and disadvantages of this procedure. They feel that it should be part of every routine physical examination of women, but that treatment for malignancy should not be instituted prior to pathologic tissue confirmation.

RADICAL SURGERY FOR ADVANCED PELVIC CANCER

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J. Michigan M. Soc., 48: 451, 1949

The treatment for cancer of the cervix is radiation; the reasons for failure might be: (1) extent of the neoplasm beyond localization to the cervix, (2) radioresistance of the neoplasm, and (3) inadequate technique of therapy. There is very little hope for prolonged control in patients by a second or third course of irradiation therapy. Since cervical carcinoma is a neoplasm which remains localized in the pelvis for prolonged periods, it would appear to be a favorable type of neoplasm for surgical attack.

It has become the policy at the Memorial Hospital to operate upon the carcinomas that persist or recur following radiation therapy, providing there is no evidence of spread beyond the pelvis. According to current opinions, these patients all were surgically untouchables.

Radical panhysterectomy with pelvic lymph node dissection was performed on 20 patients with no surgical mortality. Radical panhysterectomy with pelvic lymph node dissection, plus resection of one ureter and a portion of the bladder was done in 4 cases. Radical panhysterectomy with pelvic lymph node dissection, plus total cystectomy, complete vaginectomy with or without excision of the colon wall was performed on 13 patients with 2 deaths. Complete excision of all pelvic viscera with colostomy, bilateral ureterocolostomy was performed on 29 patients with 7 deaths. This operation was performed for recurrent cervical cancer involving bladder and rectum.

The objective of the operations is to secure palliation by removal of all macro-

In early carcinomas of the cervix, of the intra-epithelial preinvasive type, there is a prevalence of abnormal cell forms of the parabasal type. The nucleus is enlarged and tends to be hyperchromatic.

Squamous cell carcinomas of the cervix are characterized by a larger variety of more differentiated abnormal cells. Nuclear enlargement and activation, hyperchromasia, irregular fragmentation of the nucleus, engulfment, anisocytosis and anisokaryosis are more frequently encountered. Marked elongation of the cells is characteristic of well-differentiated epidermoid cancerous lesions.

Adenocarcinomas of the endometrium or of the cervix show cells of the glandular type. Vacuolization is more pronounced and the vacuoles often contain cells of the leukocytic type. Necrotic cells or stripped nuclei with an irregular grouping of chromatin granules, or single cells with an enlarged eccentric nucleus and inclusions of degenerating leukocytic elements are almost always present. Differentiation of adenocarcinoma of the cervix from adenocarcinoma of the fundus is difficult unless some of the cells retain their mucoid type.

Endometrial metaplasia is characterized by cell clusters of densely grouped normal endometrial cells; the more peripheral cells show enlargement and marked vacuolization or metaplasia. The cell groups bear a marked resemblance to adenocarcinoma cells, but may be distinguished from them by the normal nuclei and by the peripheral arrangement of the larger vacuolated or metaplastic cells.

(It was the author of this paper who, with Traut, introduced the vaginal cytologic method in the diagnosis of uterine cancer, so that certainly the paper is authoritative. So is the author's statement that it can not be considered a method of final diagnosis, and that "confirmation of smear findings with biopsy of curetted or excised tissue is recommended." This statement, coming from one who has probably had more experience with the technic than any one else, should be taken to heart by all gynecologists and cytologists. Even this short description of some of the confusing cell types which may be encountered will convince one that vaginal cytologic diagnosis is far from being a simple procedure, and leads one to doubt whether there will be in the foreseeable future a sufficient number of really expert cytologists to make this valuable screening method available to more than a small fraction of the women of the country.—Ed.)

THE DIAGNOSIS OF GENITAL MALIGNANCY BY VAGINAL SMEAR

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Am. J. Obst. & Gynec., 56: 1083, (Dec.) 1948

The authors have made and studied 6753 vaginal smears on 1709 patients. These smears were obtained, stained and classified by the methods of Papanicolaou and Traut. One hundred and fourteen patients with genital malignancy were diagnosed by smears out of a group of 124 diagnosed by pathology, a percentage of error of 8.1. False positive diagnoses were made in 34 of 1585 patients, a percentage of error of 2.1.

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The authors have briefly reviewed the advantages and disadvantages of this procedure. They feel that it should be part of every routine physical examination of women, but that treatment for malignancy should not be instituted prior to pathologic tissue confirmation.

RADICAL SURGERY FOR ADVANCED PELVIC CANCER

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J. Michigan M. Soc., 48: 451, 1949

The treatment for cancer of the cervix is radiation; the reasons for failure might be: (1) extent of the neoplasm beyond localization to the cervix, (2) radioresistance of the neoplasm, and (3) inadequate technique of therapy. There is very little hope for prolonged control in patients by a second or third course of irradiation therapy. Since cervical carcinoma is a neoplasm which remains localized in the pelvis for prolonged periods, it would appear to be a favorable type of neoplasm for surgical attack.

It has become the policy at the Memorial Hospital to operate upon the carcinomas that persist or recur following radiation therapy, providing there is no evidence of spread beyond the pelvis. According to current opinions, these patients all were surgically untouchables.

Radical panhysterectomy with pelvic lymph node dissection was performed on 20 patients with no surgical mortality. Radical panhysterectomy with pelvic lymph node dissection, plus resection of one ureter and a portion of the bladder was done in 4 cases. Radical panhysterectomy with pelvic lymph node dissection, plus total cystectomy, complete vaginectomy with or without excision of the colon wall was performed on 13 patients with 2 deaths. Complete excision of all pelvic viscera with colostomy, bilateral ureterocolostomy was performed on 29 patients with 7 deaths. This operation was performed for recurrent cervical cancer involving bladder and rectum.

The objective of the operations is to secure palliation by removal of all macro-

scopic evidence of recurrent or persistent neoplasms. The degree of palliation obtained thus far, appears to have justified the operation.

(The Brunschwig operation of excochleation of the pelvic viscera for cases of advanced, often hopeless, cervical cancer has been commented upon so often in these columns that any further remarks would be repetitious. It is not the sort of procedure that anyone could be enthusiastic about, and we shall have to wait and see whether the usually temporary and shortlived palliation which is its chief claim will be justified by the results obtained by the author and the few brave souls who are trying by emulate him.—Ed.)

UNSUSPECTED CERVICAL CANCER IN GYNECOLOGICAL PATIENTS

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Am. J. Obst. & Gynec. 57: 947, 1949

☞ Carcinoma of the cervix has been diagnosed in 14 cases in which there is no recorded preoperative suspicion of such a tumor. This represents a little over 2% of all the cervical cancers. The recorded descriptions of the cervix suggest that in almost all the cases the tumor could have been detected by biopsy prior to operation.

The patients varied in age from 30 to 56 years. In 5 cases, the cervical lesion was discovered in routine examination of total hysterectomy specimens. In 8 instances, the tumor was found in tissue removed incidental to plastic operations, and in one case, the cervical lesion was revealed in a postoperative biopsy after subtotal hysterectomy. In only one case was a preoperative biopsy of the cervix done.

Meticulous examination of the cervix with biopsy of suspect areas should precede all major gynecological operations. Because of the occasional unsuspected endocervical and endometrial cancer which it brings to light, routine curettage is a worth-while preliminary to vaginal plastic operations.

(A retrospective study of this sort is always revealing, but nor a great many studies of this sort have been made. If the original sections alone are used for re-evaluation any mistakes which are revealed would be chargeable to the pathologist rather than to the clinician, though more often it is the latter who is culpable because of lack of thoroughness in the preoperative examination of the cervix. The best illustration of this is furnished by the development of carcinoma in a residual stump after subtotal hysterectomy. When this occurs within a year or so after operation, there is little doubt that the cancer was already there, sometimes in a subclinical form, at the time of the hysterectomy. Not only curettage, but also biopsy in any suspicious cervix, should precede practically all vaginal operations. Even when the cervix appears entirely innocent, I have for some time been doing a so-called surface biopsy routinely in all vaginal operations.—Ed.)

PRE-INVASIVE CANCER OF THE CERVIX (BOWEN'S DISEASE):
REPORT OF TWO CASES

ROSA HERTZ

Proc. Roy. Soc. Med., Lond. 42: 63, 1949

The first patient was a parous woman, 63 years old, 10 years postmenopausal, who was admitted with vaginal bleeding of 3 months' duration. The cervix was grossly eroded; biopsy revealed intra-epithelial preinvasive carcinoma. Hysterectomy and bilateral salpingo-oophorectomy were performed.

The second patient was a parous woman, 51 years old, 3 years post-menopausal, who had had slight vaginal bleeding for 18 months. For the past 6 weeks, she had had post-coital bleeding. Examination revealed a polyp protruding through the os uteri. This was removed and sections showed "extreme pre-cancerous hyperplasia, classified as Bowen's disease." Hysterectomy and bilateral salpingo-oophorectomy were performed and serial cervical blocks showed pre-invasive carcinoma.

(At the present time the whole question of cancer therapy is, as has been true on a number of previous occasions in its history, in a state of flux, chiefly because of the revival of interest in the surgical treatment of selected early cases, and, in some clinics, of almost all cases, even those of very advanced stages. It will probably be a good many years before any degree of stabilization of viewpoint is again achieved.)

As regards pre-invasive lesions, there is also considerable confusion as to their proper management. If a lesion is genuinely pre-invasive, it should be curable by simple complete local excision. But the rub is that even when repeated biopsies are made, the pre-invasive nature of the lesion can not always be assumed, and a genuinely invasive process may be present in some area not reached by the biopsy. Vaginal cytology offers no help in the differentiation of pre-invasive from invasive carcinoma. It is not surprising that some clinicians have preferred to do even Wertheim operations, including bilateral removal of the adnexa, for intraepithelial lesions, and there is not the slightest doubt that in a good many cases the organs of women have been, albeit with good intentions, needlessly sacrificed because of lesions which subsequent complete studies have shown would have been easily curable by the simplest local excision. In the 2 cases reported by Hertz, the ages of the patients, both postmenopausal, would seem to have been good justification for the radical procedure carried out. There are other gynecologists, probably the majority, who in the management of carefully studied lesions which are apparently only intraepithelial, prefer to do conization, tracheloplasty or amputation of the cervix, depending on existing circumstances and personal predilections. If careful study of the removed cervical tissue should happen to reveal genuine invasive carcinoma, one can still fall back on the radical operation which most gynecologists would prefer to radiotherapy in the further management of these cases. In general, this plan appears to me as the more rational one for most cases, but there is still much floundering in this new field, and still a lot we don't know as to the nature and significance of intraepithelial carcinoma, of how often it may be a reversible process, and of its chronological and sequential relationship with genuine clinical cancer.—Ed.)

NECROPSY FINDINGS IN PATIENTS WITH CARCINOMA
OF THE CERVIX: IMPLICATIONS FOR TREATMENT

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Am. J. Obst. & Gynec., 56: 1134, (Dec.) 1948

It is generally inferred that fatality from carcinoma of the cervix is not the result of overwhelming dissemination of the disease, but rather disturbances secondary to the presence of an advanced neoplasm in the pelvis. The present study is a review of the autopsy records in the Memorial Hospital over a period of 31 years of 65 patients dying in that period of carcinoma of the cervix.

The authors have pointed out that in these cases the cancer of the cervix tended to spread primarily via the lymphatics, the periaortic nodes being first involved outside the pelvis in most instances. Half of the patients died from various causes other than wide dissemination of the disease, since necropsy revealed no gross evidence of neoplasm outside the pelvis in this group. Uremia was the immediate cause of death in 27.7 per cent of the series, and ureteral obstruction of varying degrees was present in 63 per cent of the cases. Infection, principally as peritonitis, pelvic abscess and septicemia in varying combinations appeared to be the immediate cause of death in 38 per cent of the series. Thus, uremia and infection accounted for 66 per cent of the deaths, rather than widespread dissemination of the malignancy.

Aside from eradication or restraint of the neoplasm, preservation of urinary tract function and avoidance of infection appear to be the principal problems to be dealt with for the prolongation of life in patients with cancer of the cervix.

(Death from carcinoma of the cervix, as the authors state, is most likely to occur from the regional pelvic dissemination of the disease and not from distant metastases, the terminal condition being most often stated to be uremia from blockage of the ureters, although the authors attribute an even larger proportion to infection. This does not mean, however, that distant metastases do not often occur, in spite of the fact that pelvic extension usually kills the patient before there is any clinical manifestation of the distant extrapelvic foci. At the recent meeting of the American Gynecological Society an excellent study was reported by Henriksen of the dissemination of the cancer in a large group of women who had died of cervical cancer. This paper will be published in the American Journal of Obstetrics and Gynecology later on, and will no doubt be commented on in the Survey. My recollection is that Henriksen found a surprisingly high incidence of distant metastases, something like 37 per cent, although the immediate cause of death, most often uremia, was due to the pelvic dissemination by the well-known lymphatic routes. It seems to me that this factor of distant metastases can not be overlooked by those who, like Brunschwig, often do the very radical "All American" operation of removing all the pelvic viscera in advanced cases of cervical cancer. These operations, true enough, are not offered as curative, being done chiefly with a view of lessening the sufferings of the patient in the terminal stages of the disease. If distant metastases are already present in a considerable proportion of cases, as Henriksen's studies indicate, it is easy to see that such operations would not be curative even if it were possible to clear out the cancer from the pelvis.—Ed.)

LEIOMYOSARCOMA OF THE UTERUS: REPORT OF 16 CASES,
1917 TO 1948

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Am. J. Obst. & Gynec., 56: 1048, (Dec.) 1948

The writers have reviewed 16 cases of leiomyosarcoma of the uterus occurring in a 30-year period at the Methodist Hospital. The incidence of this tumor was 0.69 per cent of the leiomyomas and 0.04 per cent of all pathological uteri examined. Fourteen of the 16 cases could be differentiated from leiomyoma on gross examination because of difference in consistency, difference in color, loss of fasciculation, or gross evidence of invasiveness. It was felt that these tumors could be classified into 2 distinct groups histologically, which were designated as unequivocal leiomyosarcoma and low grade leiomyosarcoma. The first group showed all the classical histologic features of malignancy, while the second group showed less striking evidence of malignancy. However, the low grade type may recur in contiguous structures after relatively long periods and may show local invasion.

Analysis of this series of cases showed that the average age of onset was 47.2 years. The most prominent symptoms were those referable to the menstrual cycle. The mortality rate was 54.5 per cent with death due to metastasis within 2 3/4 years. The danger of a too-limited surgical approach is illustrated by the cases of local recurrence which were due to pelvic spill of the tumor. The authors also warn against tearing this friable tumor, which might result in implantation of spilled tumor cells. In 14 of the 16 cases the leiomyosarcoma arose from a pre-existing leiomyoma. In this group, metastasis was observed by blood stream and by direct extension. Of the 11 cases which had adequate follow-up, 3 are living and well without recurrence. Two cases had to have further operative procedures for recurrence but are now living without further evidence of disease. This study suggested that leiomyosarcoma arising in the fundus rarely recurred in a retained cervical stump, providing the site of excision was well below the involved area. In spite of this, the authors believe that a total hysterectomy and bilateral salpingo-oophorectomy is the procedure of choice when the patient's condition warrants it. 4 figures.

(The incidence of sarcomatous change in myoma, as given by the authors, 0.69 per cent, is not much different from that reported from the Laboratory of Gynecological Pathology at John Hopkins Hospital by Novak and Anderson in 1937. Our figure, based on a study of 6981 myomas, was 0.56 per cent. Other authors have reported a somewhat higher incidence, Kimbrough's figure being 1.02 per cent, that of Franz 0.64 per cent, and of Frankl 2.02 per cent. In only 39 of our 59 cases did the sarcoma arise in a myoma, in contrast to the 14 out of 16 reported by the authors of the above paper. They properly lay stress on the suspicious gross appearance of myomas which are undergoing sarcomatous change, and this emphasizes the importance of opening such tumors, especially those of rather soft consistency, as soon as they are removed, and before the abdomen is closed. If the cut

surface is firm and of characteristic trabeculated or whorl-like appearance, one need have little fear of sarcoma. If on the other hand, the tumor is of soft pulpy consistency, with often rather ragged cavity formation, one should suspect sarcoma. The trabeculation is often lost in simple hyaline degeneration, and the consistency is apt to be soft, but the amorphous or gelatinous appearance is different from the "raw pork" picture often seen with sarcoma.

When the gross examination indicates a suspicion of sarcoma, a total hysterectomy should always be done if in any way possible. There are few surgeons who have not had the disconcerting experience, in the days when the subtotal technic was the popular one, of receiving a report of sarcoma in cases thought to be simple myomas. Even more distressing are the occasional cases of sarcoma in tumors removed by myomectomy. Many difficult problems of judgment as to further treatment thus arise, though less frequently in these days of total hysterectomy. Each such problem must be decided individually, on the basis of such factors as the extent of the operation which has already been done, the proximity of the sarcomatous disease to the line of amputation if a subtotal operation has been done, the microscopic characteristics of the sarcoma, etc. In some cases further and more radical operation is advisable, in others radiation may be selected, and in a small proportion of the low grade sarcomas no further treatment other than careful observation.

The mortality rate reported by the authors, 54.5 per cent, is better than that reported by most authors.—Ed.)

MESONEPHRIC REMNANTS IN THE CERVIX

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Am. J. Obst. & Gynec., 56: 23, (July) 1948

It is well known that certain portions of the mesonephros may persist near the ovary and in the broad ligament and the vagina of the adult human female, but that they may persist in the cervix is far less commonly realized. It has been shown that the mesonephric duct as it enters the lower uterine segment and cervix dilates to form a distended ampulla located in the middle muscle layer of the lateral cervical wall. The duct persists in about 20 per cent of fetuses and the ampulla forms a cleft-like cavity which has, in cross section, slight bends and curves and the beginnings of a few rather large diverticula. The remnants may be found in the adult cervix either as persistent fetal structures or as new growths arising from fetal residuals. The characteristic histological appearance of mesonephric remnants in the cervix is that of small tubules or canaliculi, lined by a typical low columnar nonsecretory epithelium consisting of cuboidal cells containing a translucent pale cytoplasm and large, well-staining, ovoid or round nuclei. These tubules are usually discovered on routine sections of the cervix and can be differentiated from cervical glands. Their course is generally longitudinal, though corkscrew, and there is usually a scattering of surrounding musculature and stroma similar to that which surrounds the fetal mesonephric duct.

Three major pathological conditions may arise from these remnants, namely,

cysts, adenomatous hyperplasia and adenocarcinoma. The cysts are usually small (rarely over 2.5 cm. in diameter) and are usually without significance. Adenomatous hyperplasia occurs as a conglomerate mass of closely packed small tubules which is usually found deep in the cervical musculature. These rarely progress to tumors of appreciable size. Occasionally, the tubule cells will show some secretory activity but usually the tumor is discovered incidentally. In 1192 cervical specimens examined by the author, 4 instances of adenomatous hyperplasia of mesonephric remnants were found.

Adenocarcinoma of these remnants manifests itself as a tumor mass in the anterolateral or posterolateral midcervical walls. Microscopically, masses of gland-like tubules are seen, unorganized in arrangement and lined by many layers of neoplastic cells. The position of the tumor plus other evidence of mesonephric remnants aids in establishing the diagnosis. In the author's series of cases, one adenocarcinoma of the mesonephric duct was found. 16 figures.

(This paper should serve a well-worthwhile purpose in calling attention to the fact that mesonephric vestiges may occasionally be found in the cervix. This fact has been known for a good many years, but, since the occurrence is relatively rare it is not surprising that pathologists are often mystified to find these structures and that misinterpretations are often made. The persistent mesonephric duct is usually found just at the outer margin of the uterine and cervical wall, but the remnants may at times be well within the substance of the cervix, producing such pictures as the author describes. The rather tubular pattern as well as the character of the epithelium makes the differentiation easy. Incidentally, similar mesonephric vestiges may also be found in the lateral fornix of the vagina and secondary infection may give rise to ulcerative lesions which may simulate carcinoma. I recall 2 such cases, the biopsy revealing typical adenomatous mesonephric tubules in the base of the ulcer.—Ed.)

THE CONSERVATIVE MANAGEMENT OF ENDOMETRIOSIS

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Surg. Clin. N. America, 29: 583, 1949

Novak defined endometriosis as "the condition in which tissue resembling more or less perfectly the uterine mucous membrane occurs aberrantly in various locations in the pelvic cavity." Endometriosis is, in the main, a disease of young women. Meigs drew attention to the fact that endometriosis was increasing in frequency and suggested delayed marriage and the lack of early and frequent childbearing as possible factors. The condition is one of the most common pelvic lesions found at operation in women during active menstrual life. Endometriosis occurs more frequently among patients in private practice than those in a general hospital population.

The authors report 6 cases of endometriosis treated with testosterone pellet

implantation with successful alleviation of symptoms for periods of 6 to 8 months. Satisfactory amelioration of the syndrome may also be obtained with parenteral and oral administration of testosterone. These are particularly useful as a therapeutic test before pellet implantation.

The treatment of endometriosis is difficult. The choice lies among hormonal therapy, surgical intervention, and irradiation. In young women with mild complaints, surgery may be postponed with the hope that the pelvic condition will subside, or that pregnancy will occur. Most authors agree that every attempt should be made to conserve ovarian and childbearing function. Deferring laparotomy until the patient is older results in fewer reoperations and better end results.

Patients with endometriosis frequently are sterile. In the presence of endometriosis and pregnancy, abortion, premature labor and extrauterine pregnancy often occur. The authors searched the literature and concluded that approximately one third of patients with endometriosis treated conservatively can successfully conceive, and that the majority of such patients have a normal pregnancy. In the case of pregnancy complicated by ureteral endometriosis, the patient became pregnant after 3 years of androgen therapy.

Many authors have attested to the merits of androgen therapy. According to Hirst, the positive values appeared to be the rapid reduction of pain, tenderness and swelling of grossly cystic ovarian endometriomas. Androgens will not cure endometriosis and have but a temporary action. The authors have used pellet implantation in many patients with excellent results. Following a short therapeutic test with parenteral or oral androgen therapy, as many as three 75 mg. pellets of testosterone may be implanted subcutaneously. This method of therapy has produced satisfactory alleviation of symptoms preoperatively and has controlled residual or recurrent endometrial lesions following conservative surgery. There was no difficulty in the control of dosage; arrhenomimetic phenomena were mild. The advantage of the pellet mode of therapy is the convenience afforded the patient by a single treatment.

(See comment on following abstract of paper by Bacon.—Ed.)

RESULTS IN 138 CASES OF ENDOMETRIOSIS TREATED BY CONSERVATIVE SURGERY

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Am. J. Obst. & Gynec., 57: 953, 1949

In endometriosis of sufficient degree to warrant laparotomy, a major problem is whether or not to conserve menstrual function and childbearing ability. The author reviews 214 cases of endometriosis treated by conservative surgery from

1905 to 1941 inclusive. Of these, 138 cases of intra-abdominal, pelvic endometriosis, diagnosed grossly and histologically, were treated by laparotomy at which the childbearing function was anatomically preserved.

Sixty-eight (49.3%) of the patients were relieved of symptoms; 29 (21%) were partially relieved; and 41 (29.7%) were failures, requiring later radical surgery or radiation. One hundred twelve patients in the series were married and under 40 years of age; of these, 30 (26.8%) delivered a total of 39 living children. Of the 30 patients who had children, 22 were classed as being relieved of their symptoms, 3 as partially relieved, and 5 as failures. The average interval between operation and delivery was 2.7 years.

Of the 41 patients classed as failures, 26 were treated with hysterectomy, 5 by miscellaneous pelvic laparotomies, 4 with radium and 6 with x-ray. Pathologic diagnosis was available in 20 of the cases treated by hysterectomy; of these, 9 showed recurrent endometriosis. The findings in the remaining 11 cases include adhesions, chronic salpingitis and oöphoritis, retention cysts and fibroids, but no endometriosis was demonstrable.

The prognosis for symptomatic relief and future pregnancy does not seem to be affected by age, symptomatology, the location and extent of the disease, or the magnitude of the conservative operation performed. The presence of a considerable amount of endometriosis is not a contra-indication, from the point of view of prognosis, to a conservative operation.

(The conservative plan of treatment advocated by the authors of both of the papers above will be endorsed by all of us, although there are few surgical conditions which in individual cases may pose more difficult problems of judgment. In the first place, endometriosis is often of rather academic importance, as when tiny islands of aberrant endometrium are unsuspectingly found on the surface of the ovary or elsewhere on the pelvic peritoneal surface in the course of operations done for entirely different and more important lesions, such as myoma. These endometrial lesions have caused no symptoms and a large proportion of them will cause none in the future; so that the simplest type of local excision or cautery destruction is all that is necessary. At the other extreme there is a group of cases in which both ovaries are the seats of large endometrial cysts, with large and perhaps multiple nodules in the uterosacral ligaments and with the rectum welded to the neoplastic infiltration of its walls. In this group it would be false conservatism to try to retain any ovarian tissue.

The largest number of cases, however, is of intermediate type, with perhaps an endometrial cyst in one ovary, while the other is normal or shows only a few small surface islets of endometrium. Here there is no question as to the indication for conservatism and the generally good results of this policy, not only as regard the patient's well-being but also the frequency of subsequent pregnancies, is shown in the results reported by Bacon. There are of course some exceptions and a later more radical operation may be necessary, but this will seem far less tragic to the patient if she has been fortunate enough to have a baby in the meantime. All sorts of modifying conditions may have to be considered in addition to the age of the patient, her social status, and her attitude toward future pregnancies. For example, a troublesome problem may be presented by cases in which one ovary is easily conservable, but the utero-sacral ligaments are extensively involved, and the rectum welded to the back of the cervix and uterus. Utero-sacral nodules, histologically often adenomyomatous, are sometimes readily excisable, but in other cases, where they are numerous, large and practically incorporated with an adherent rectum, complete removal of endometrial tissue is practically out of the question. Each case must be decided on a purely individual basis.

Endometriosis, in my experience, is not by any means always as painful a disease as it is commonly pictured. Every gynecologist encounters not infrequent cases in which, through the presence of definite uterosacral nodules combined perhaps with an adherent enlarged ovary, he can be quite sure as to the existence of pelvic endometriosis, and yet the patient may have little or no dysmenorrhea, pelvic discomfort, dyspareunia or other symptoms. The same statement may be made of a good many cases of a residual or recurrent endometriosis following previous operation for this disease. Such cases can be treated expectantly, especially in women approaching the middle period of life.

If, in cases of this anatomical type, a patient has moderate or rather severe dysmenorrhea, there are some, like Greenblatt and Suran, Hirst and others, who are quite enthusiastic about androgen therapy. This, however, is only temporary in its effect, and would thus have to be continued indefinitely. As for pellet implantation, I confess I have never been a pellet enthusiast for any gynecological indication, especially in these days of effective and more flexible oral therapy. I suppose it is a matter of individual reaction and preference, but I find that there are few cases in which the patient can not be made reasonably comfortable by simple analgesias. If the symptoms become severe enough to constitute an important problem to the patient, surgery is often necessary, not infrequently combined with presacral neurectomy.—Ed.)

THE ADNEXA

TWISTED HEMATOSALPINX

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Am. J. Surg., 77: 661, 1949

Hematosalpinx may be divided into 3 groups, according to origin: (1) gynaesthesia, (2) cases attributable to bleeding from a ruptured blood vessel into an occluded tube, and (3) cases attributable to a disturbance in blood supply due to torsion. In the etiology of torsion of the tube, there are predisposing factors and twisting forces. The predisposing factors may be divided into those related to pathologic conditions in the abdomen and those related to the part which is twisted. The twisting forces can operate from without or from within the abdomen.

Diagnosis of a twisted tube is a difficult matter. The twisted tube must be differentiated from ureter stone, ectopic pregnancy, acute appendicitis and salpingitis. The history of repeated attacks of pain in the lower abdomen seems to be more significant diagnostically than all other symptoms. Salpingitis can be excluded by the absence of high temperature. Pelvic examination may aid in excluding appendicitis.

The author reports one case of twisted hematosalpinx. Operation was performed without a definite diagnosis preoperatively. An originally normal right tube had undergone acute axial torsion resulting in strangulation with consequent hemorrhagic changes. There was a firm adhesion across the pelvis due to a previous operation. The right mesosalpinx was extremely long, forming a pedicle which was well predisposed for torsion. The tube was abnormally long.

In this case the intraperitoneal forces and the factor of tubal peristalsis seem to be of great importance. Since the long tube on the elongated mesosalpinx had a wide range, the tube was caught in the adhesion across the pelvis; the adhesion exerted pressure on the tube, blocking the circulation and activating the twisting forces for hemodynamic torsion.

(Either a normal tube or a hydrosalpinx may undergo torsion, the latter probably being the more frequent, and the preoperative diagnosis is, as the author states, very difficult and is not often made. If torsion of the adnexa is suspected, one is more likely to think of torsion of the pedicle of a small ovarian cyst. When a normal tube undergoes torsion, the ovary may be included in the process. That this is true is indicated by the occasional case in which operation in women who have had no previous laparotomy may reveal what at first sight may seem to be a congenital absence of one tube and ovary. In the cases of this type which I have seen, however, closer inspection shows the presence of a short stump of tube, as if there had been a previous tubal amputation. There is no doubt that in such cases there had been, perhaps in early or possibly even fetal life, a spontaneous torsion of the tube and ovary, with later complete absorption of the twisted-off organs. There is

ample evidence in the literature that even with fairly large ovarian cysts, spontaneous amputation and later resorption of the adnexa may occur, but for detailed discussion of twisted hematosalpinx, see editorial note by Eastman in August issue of Survey, page 498.—Ed.)

VASCULAR PATTERNS IN THE HUMAN OVARY

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Am. J. Obst. & Gynec. 57: 842, 1949

Knowledge of the physiology of the uterus has sufficiently advanced so that certain functions can be ascribed to endometrial spiral arterioles. A similar situation exists with respect to the spiral arteries of the ovary. In 1947, it was observed in the ovary of the rabbit that the arterial branches in the hilus are spirals of gradually diminishing diameter. When the size of the ovary was increased by injection of chorionic gonadotrophin, the helical spirals became extended. The effect is transient; regression occurred following a decrease in ovarian size. Spiral configuration is restored by the 6th day following intravenous injection of the gonadotrophin. It has been suggested that distortion of the spiral artery might contribute to cystic development through altered local hemodynamic relations in the ovary during the active growth phase of the follicle under stimulation of the gonadotrophins. The association between distortion and cysts suggests that spiral arteries in the ovary may serve to regulate the blood pressure within the ovary.

Sixty sets of ovaries were injected with vinylite plastic and the vascular tree was isolated following the use of a corrosion bath. Injection was made through the ovarian and uterine arteries in adult ovaries. In infant and fetal specimens, injection was made by way of the lower aorta.

The main ovarian artery is undulant, tortuous, with a degree of flattening; its branches proceed from the hilus into the ovary in a parallel manner. Primary, secondary, and tertiary branches arise from the main artery in the hilus. The primary trunks are tortuous or undulant with an occasional spiral. The degree of crowding among the branches is dependent upon the presence and size of cysts and corpora lutea in the ovary. A greater tendency to spiralling is noted in the smaller vessels.

Spiralling occurs in the form of a helix with a gradually diminishing diameter. The tightness of the spiral is influenced by the presence or absence of pathology, by the presence of cysts, large Graafian follicles or corpora lutea, by the menopause, and by the engorgement of the venous system of the ovary. Evidence that an extension of the spirals and flattening of the ovarian spiral arteries occurs in relation to the presence of localized structures within the ovary (follicles, corpora lutea, and cysts) has been observed.

In ovaries of patients past the menopause, sparse, thin, and widely spaced arterial branching of the primary, secondary and tertiary ovarian arteries was observed. This picture suggests the action of estrogens upon the growth and development of the primary, secondary, and tertiary branches of the ovarian artery.

From the 7th month of gestation until a short time after birth, growth and development of the vascular pattern in the ovary may be noted. At 3 months of age, there is no trace of spiralling. It would seem that the presence of spiralling, and its regression in fetal and infant ovaries, is dependent on a maternal hormonal influence. It is suggested that maternal hormones may stimulate the development of spiralling and branching of the primary, secondary and tertiary arteries in the ovary beginning late in fetal life. The action is most marked about one week after birth. Regression takes place over a period of several months.

The casts of ovarian veins are different morphologically from those obtained from the arterial system. Within the ovary, the veins end in small, straight channels that are never spiralled.

(The important role played by the spiral arterioles of the endometrium in menstruation is now well established, although there are still gaps in our knowledge, especially as to the nature of the liaison between this vascular apparatus and the motivating hormones. After all, this endometrial vascular apparatus can be expected to be of prime importance in such a vascular phenomenon as menstrual bleeding. It can not so readily be hypothesized that the spiral arterioles of the ovary would play an important part in ovarian physiology. This spiral apparatus was discovered many years ago, but rediscovered only recently by the senior author of this paper (Reynolds), who has made valuable contributions to various endocrine problems, especially that of the hormonal control of uterine motility.

A careful reading of the present paper leaves me rather confused as to whether the authors wish to emphasize that the variations in spiral coiling may actually be responsible for certain histological changes, or whether, as I rather think is their view, the variations in the ovarian spiral vessels are merely the result of the presence of such structures as large follicles, corpora lutea and cysts. Interesting as their studies are, and potentially important though they may be considered, for the present I would feel that they are in the academic stage, with no immediate practical lesson for the gynecologist.—Ed.)

AGING PROCESSES IN THE OVARIES OF MICE BELONGING TO STRAINS DIFFERING IN THE INCIDENCE OF MAMMARY CARCINOMA

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Arch. Path., Chic., 46: 401, 1948

Four periods in the life of the mouse were distinguished: (1) from birth to 9 months of age, (2) from 10 to 14 months, (3) from 15 to 19 months, and (4) from 20 months or older.

A decline of the full development of the follicles sets in in period 3 and becomes

more pronounced in period 4. Although differences in this process occur between different strains, there is no parallelism between these differences and the likelihood of the individual to develop mammary carcinoma. The follicles may be very large, and cystic or hemorrhagic, or cystic and hemorrhagic simultaneously. In some cases, dilatation of the follicles appears to be the primary process, while in others, hemorrhage is primary. In mice, primordial follicles may be seen in the deeper parts of the ovary, even in older animals.

Degeneration of the corpora lutea has 3 stages. These are hyalinization, gelatinization, and solution. The hyalinization and gelatinization of corpora lutea increase in frequency and intensity up to period 4.

In general, the interstitial gland increases in size with increasing age. In periods 3 and 4, the cells tend to become more or less vacuolated and to accumulate yellow or brown pigment. The interstitial gland tissue was derived mainly from the theca interna of atretic follicles. The author believes that regressing corpora lutea may become a part of the interstitial gland. With advancing age the germinal epithelial and medullary ducts increase in number. In periods 3 and 4, they undergo coiling, formation of adenoma-like structures, vacuolation of duct cells, and apparent or real transitions leading to lutein-like interstitial gland tissue. Cysts derived from the medullary ducts and from the germinal epithelium increased with age.

With increasing age, mitotic figures appeared in medullary as well as germinal epithelial ducts, in adenoma-like structures, in lutein-like tissue, and in fully developed interstitial gland tissue. Ducts accompanied by lutein-like interstitial gland could penetrate through the surface of the ovary into the surrounding fat.

Processes of hyalinization occurred in and around arteries and capillaries. They increased in frequency with increasing age and were partially associated with processes of hyalinization which took place in corpora lutea.

OVARIAN PREGNANCY: A CASE REPORT

JOHN P. BOLTON

White Cross Hospital, Columbus, Ohio

Ohio M. J., 45: 353, 1949

According to Spiegelberg, the four postulates for the diagnosis of ovarian pregnancy are as follows: (1) the tube on the affected side must be intact and separate from the ovary, (2) the fetal sac must occupy the position of the ovary, (3) the pregnancy must be connected to the uterus by the ovarian ligament, and (4) definite ovarian tissue must be found in the sac wall.

The patient, aged 20, was admitted with history of sharp pain low in the right side, faintness, and abdominal swelling and tenseness. Her last normal menstrual period was approximately 6 weeks prior to admission. At examination about 14

hours after the onset of pain, the abdomen presented abnormal sensitivity, most pronounced on the lower right side. There was only slight rigidity. On pelvic examination, the cervix was normal in size and appearance, except for a blood-tinged non-purulent mucus extruding from the external os. The uterus was slightly enlarged, and there was extreme tenderness in the cul-de-sac toward the right side. The tentative diagnosis was right ectopic pregnancy, ruptured, with profuse intra-abdominal hemorrhage. At operation, the right ovary was about 6 cms. in diameter and contained a cystic structure which appeared to contain blood or placenta. On the inferior surface of the ovary was a bleeding crater. A thin serous sac was noted in the clotted blood contents of the abdominal cavity. A post-operative diagnosis of ectopic pregnancy, right, ovarian, ruptured, was made. Sections of the ovary through the area of bleeding showed a deeply placed corpus luteum formed of well developed luteal cells. External to this corpus luteum was a hemorrhagic mass infiltrated with syncytial cells. Within the hemorrhagic material of the ovary there were multiple young chorionic villi. Sections of the separate sac showed it to be a simple peritoneal cyst. Microscopic diagnosis was ovarian pregnancy with massive hemorrhage. The patient was discharged in good condition on the 9th post-operative day.

Ovarian pregnancy has no preoperative differential diagnosis; the symptoms are those common to tubal pregnancy. Termination of extra-uterine pregnancies may be: (1) early death of the fertilized ovum with resorption, (2) development to an advanced state with delivery at term by laparotomy, and (3) rupture may occur, and the fetus may die or become reimplanted and continue to grow. Every case of ruptured extra-uterine pregnancy should go to surgery promptly.

(See comment on following abstract of paper by Deweese.—Ed.)

OVARIAN PREGNANCY

W. J. DEWEESE

Bimidji, Minnesota

Minnesota M., 32: 272, 1949

Ovarian pregnancy is the rarest of the primary forms of gestation except for the cervical and abdominal. It was first reported in 1682 by Maurice. Approximately 81 cases of primary ovarian pregnancy have been reported. The incidence has been estimated at one in 25,000 pregnancies, and to be from 0.7 to 1.07% of all ectopic pregnancies. Two types of ovarian pregnancy have been described: the primary, in which the ovum is fertilized while it is still within the follicle; and the secondary, where the ovum is fertilized after its release from the follicle and subsequently implants upon the surface of the gonad.

Retrograde movement of the fertilized ovum, and tubal abortion have been considered as possible mechanisms favoring ovarian nidation. Endometriosis

of the ovary has been mentioned in this connection. Implantation and placentation do not differ greatly from those of intrauterine pregnancy except for the absence of true decidua.

The usual course of ovarian pregnancy is rupture of the ovary and extrusion of the products of conception within the first trimester. However, 38 cases have been reported to have gone to the age of viability of the fetus (7 months). Symptomatically, ovarian pregnancy resembles tubal gestation. Pathologically, the 4 criteria of Spiegelberg must be satisfied before making the diagnosis.

The author reports the case of a 24 year old white woman who had abdominal pain and vaginal bleeding 5 weeks after her last period. Laparotomy revealed a ruptured right ovarian pregnancy. The fetus was not found.

(An increasing number of cases of ovarian pregnancy are being reported from year to year, but it still is to be looked on as one of the rare types of ectopic implantation. At first thought this may seem strange, when one considers that the tubes, if one may judge from animal experimentation, may swarm with spermatozoa shortly after coitus, and there would seem to be little doubt that many of these pass out through the fimbriated end of the tube. One might therefore expect that the ovum would be more frequently pounced upon by the swarm just as it is extruded from the follicle, or even before this, when the follicle wall has perforated but the ovum is still within the follicle cavity. That the latter undoubtedly occurs in at least some cases is shown by the fact that in some early cases the small implantation area is seen within a follicle which has undergone transformation into a corpus luteum. When implantation occurs on the ovarian surface, it is at least theoretically possible though impossible to prove, that an egg fertilized in the outer end of the tube may be dropped back on the ovarian surface, with later implantation.

It is difficult to do more than speculate as to why and how ovarian pregnancy arises, especially since the majority of cases come under observation at a stage too late to throw light on these points. Indeed, in many cases such pregnancies at operation present as conglomerate, hemorrhagic adnexal masses, so that, even though one may strongly suspect a primary ovarian situs, it is simply impossible to establish the Spiegelberg criteria beyond doubt.

As to why ovarian pregnancy does not occur much more frequently than it does, in view of the migratory proclivities of the spermatozoa, my own concept has always been that this could be logically explained by the fact that the ovum as it exists in the follicle and immediately after extrusion, is ordinarily immature and thus not-capable of fertilization, as is the ovum in transit through the tube. It appears to be established that, while the first polar body is given off within the ovary, the second, after the essential reduction mitosis, is characteristically extruded in the outermost portion of the tube. That there are occasional departures from this rule, and that full maturation may occur within the follicle, would seem to be established beyond question by the fact that in rare cases ovarian pregnancy does occur.—Ed.)

OVARIAN TUMORS AND UTERINE BLEEDING

M. A. BAYLE AND R. R. GREENE

*Dept. of Obstetrics and Gynecology, Northwestern University Medical School,
Chicago, Ill.*

Am. J. Obst. & Gynec., 57: 984, 1949

It has been assumed that some hormone-producing tumors of the ovary cause abnormal uterine bleeding, and it is widely accepted that nonhormone producing tumors may occasionally have the same effect. Several authors have granted that nonhormone producing tumors may be associated with abnormal bleeding. However, they have suggested that the bleeding was due to an unrecognized granulosa-cell tumor, or possibly a misinterpreted functioning neoplasm.

Tissues were available from 154 patients with cystic or solid nonhormone-producing ovarian tumors. Only 74 tumors with accompanying uteri were available. Twenty-seven of the tumors were removed from post-menopausal women; the remaining 47 were considered to be premenopausal although 32 of them were 40 years of age.

In 74 patients, 15 (20%) had abnormal bleeding. In all but 3 of these patients, other factors than the ovarian tumor were found which could explain the bleeding. The authors were unable to find any relationship between the tumors and the endometrial picture. It seems unlikely that nonhormone-producing ovarian tumors, per se, cause abnormal uterine bleeding.

Of the postmenopausal patients, 44% showed atrophic endometrium; in 25.9%, the endometria had areas that resembled the estrogenic phase of a normally cyclic uterus; 7.4% had endometria identical to that of the normal proliferative phase; the remaining 22% had hyperplastic endometria. Thus, over half of these postmenopausal women had endometria that showed evidence of estrogenic stimulation.

(With the exception of the feminizing functioning group, ovarian tumors exert no characteristic effect upon the amount of menstrual flow. It is obviously harder to establish this in women during menstrual life, because certainly both benign and malignant ovarian tumors can at times be associated with menstrual excess, usually moderate. In most cases this is explained by other associated factors, but it is entirely possible that in an occasional case the hyperemia or pressure produced by the tumor may be concerned. The influence of ovarian tumors in producing postmenopausal bleeding can be studied with somewhat greater precision, and here it is possible to substantiate the statement made at the beginning of this editorial comment. Even advanced ovarian carcinoma is usually associated with no uterine bleeding. If the latter occurs, it is likely to be due to endometrial metastasis, and in other cases to some such cause as senile endometritis, postmenopausal bleeding, or endometrial polyp. I recall that in the early days of our knowledge of Brenner tumors a prominent German gynecologist, Schiffman, published a number of papers insisting that Brenner tumors possess a hormone function, and reporting a definite hyperplasia of the endometrium in a small group of such cases. We know now however, that even striking hyperplasia can occur postmenopausally in women who have no tumors in any organ. On the other hand, the vast majority of the now large number of Brenner tumors which have been

studied show no hyperplasia and no bleeding, the endometrium being usually of senile type. In other words, when Brenner tumors and endometrial hyperplasia are combined, the relation is coincidental only.

Incidentally, no longer can the finding of postmenopausal hyperplasia in itself justify the diagnosis of a feminizing tumor of the ovary, granulosa-cell or thecoma. It was formerly thought that even when no tumor could be palpated, the finding of postmenopausal hyperplasia would justify laparotomy, and that a small granulosa cell tumor or thecoma would be revealed. Much more frequently, however, no tumor of any kind is found, the hyperplasia being due to estrogen which has its source from some extra-ovarian source, probably the adrenal cortex.—Ed.)

OVARIAN AGENESIS (TURNER'S SYNDROME) REPORT OF A CASE WITH POST MORTEM FINDINGS

JAMES M. MOSS AND KARL F. MENK

University of Virginia Hospital, Charlottesville, Va.

Virginia M. Month., 76: 186, 1949

The patient was a 26 year old white married woman who was admitted with typhoid fever. Family history was non-contributory; she was the oldest of 5 children and had always been smaller than the other children of her age. She had never had any mammary development or cyclic uterine bleeding. She had never had any endocrine treatment.

Physical examination showed height 58 inches, weight 85 pounds. There were many pigmented nevi scattered over the skin. There was a fold of skin extending from the mastoid region to the acromial process on the right. The carrying angle at the elbows was slightly increased. The pubic hair was sparse, as was the axillary hair. The breasts were flat, the nipples slightly protuberant. The external genitalia were hypoplastic. The vagina was smaller and less elastic than normal; the uterus was small and of juvenile proportions; no ovaries or other masses could be palpated in the adnexal regions. The patient died 10 days after admission. The clinical diagnosis was typhoid fever, with death due to pulmonary edema; ovarian agenesis, dwarfism, cubitus valgus, and webbed neck.

At autopsy a fused double kidney was found on the left. Both adrenal glands were in their normal position; the left weighed 11 gms., the right 7.3 gms. The uterus measured 6 x 4 x 2 cm., the cervix made up about half the mass. No ovaries could be located; the tubes and vagina were small. The pancreas, thyroid, parathyroids, and pituitary glands were grossly normal. Microscopic examination of the vaginal epithelium showed moderate cornification with an average thickness of 6 cells. The uterine endometrium was hypoplastic. The Fallopian tubes were immature and no ovarian tissue was demonstrated in sections of the adnexal regions. Sections of the pituitary showed eosinophilic hyperplasia of the anterior lobe. Anatomical diagnosis was (1) primary ovarian agenesis; absence of ovaries, immaturity of genitalia and breasts, shortened stature, sparse pubic and axillary hair, cubitus valgus, webbed neck, congenital anomaly of kidneys, acidophilia of pituitary, (2) typhoid fever, and (3) pulmonary edema.

The fundamental defect of the endocrine system in this syndrome is a congenital absence or failure of development of the ovaries. In the absence of sufficient estrogens in the blood, the anterior lobe of the pituitary is stimulated to secrete an excessive amount of follicle-stimulating gonadotropic hormone. This results in an increased excretion of the gonadotropic hormone in the urine. Urine examination is one of the most valuable laboratory aids in the diagnosis of this syndrome. Attempts to explain the shortened stature on an endocrine basis have not been entirely satisfactory. Estrogen administration to these patients results in uterine growth, vaginal cornification, and pigmentation and growth of the nipples. Thus, it is believed that the hypoplasia of the genitalia is on an endocrine rather than on a genetic basis. No explanation has been offered for the frequent association of cubitus valgus, webbed neck, and other congenital anomalies with ovarian agenesis. The osteoporosis found in many of these patients has been attributed by Albright to the absence of estrogens.

(The clinical syndrome in cases of ovarian agenesis, with or without the extra added feature of osteoporosis described by Albright in at least some of them, is rather distinctive and quite a number of cases are now to be found in the literature. Until very recent years it was commonly stated in the textbooks that congenital absence of the ovaries was exceedingly rare, being found chiefly in association with fetal monstrosities of one sort or another. This apparently is not true, although, as the authors' case illustrates, there are often other associated congenital anomalies. I do not believe that the authors can mean that the hypoplasia of the genitalia is of endocrine rather than genetic origin, if they include the ovary among the genital organs. I suppose they refer only to the genital tract itself (tubes, uterus and vagina) and on this point there would seem to be no question that the absence of ovarian hormones explains the uterine underdevelopment. In one or two cases in which I have had the opportunity of microscopic examination of the adnexal area, I felt that the ovary was not completely absent but exceedingly rudimentary, the gonadal area showing a fairly typical ovarian stroma but with little or no evidence of follicle apparatus. Such cases would seem to represent extreme hypoplasia rather than complete agenesis of the ovaries.—Ed.)

PAPILLARY CYSTADENOCARCINOMA OF THE OVARY TREATED
WITH LARGE DOSES OF TESTOSTERONE PROPIONATE.
REPORT OF A CASE

BYRON D. ST. JOHN

Port Washington, N. Y.

J. A. M. A., 140: 1076, 1949

The patient was a 43 year old woman with complaint of swelling and tenderness of the lower part of the abdomen. Three months prior to examination, she had a fibroadenoma removed from the left breast. Physical examination was normal except for the abdomen and pelvis. The lower portion of the abdomen was swollen and distended. The liver was not significantly enlarged. Pelvic examination revealed a mass in the hollow of the sacrum which felt like a pregnant uterus.

studied show no hyperplasia and no bleeding, the endometrium being usually of senile type. In other words, when Brenner tumors and endometrial hyperplasia are combined, the relation is coincidental only.

Incidentally, no longer can the finding of postmenopausal hyperplasia in itself justify the diagnosis of a feminizing tumor of the ovary, granulosa-cell or thecoma. It was formerly thought that even when no tumor could be palpated, the finding of postmenopausal hyperplasia would justify laparotomy, and that a small granulosa cell tumor or thecoma would be revealed. Much more frequently, however, no tumor of any kind is found, the hyperplasia being due to estrogen which has its source from some extra-ovarian source, probably the adrenal cortex.—Ed.)

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from the uterus. The mass was removed, a few ounces of fluid were found in the pouch of Douglas, but no adhesions or other signs of a fully developed endometriosis were noted.

Both ovaries were enlarged. Section showed typical serous adenofibroma on either side. Groups of acini of a wavier outline surrounded by a loose, cellular stroma infiltrated with blood were seen at certain areas on the surface of the ovary. In one of these areas, the entering connective tissue fibres alter, becoming finer, more subdivided and less disposed to occur in bundles. A ripening follicle was observed. There was no evidence of old hemorrhage and the prussian-blue reaction was negative. The endometrium was in the follicular phase and contained some mitoses. The ovarian changes were interpreted as endometriosis.

The adenofibroma was presumably present before the menopause; it is unlikely that the endometriosis was present then. The serosal origin of both conditions, which the sections suggest, seems the only possible interpretation.

(The description of the findings indicates the presence of an ovarian adenofibrosis and an associated endometriosis, but the assumption of a partial differentiation of the adenofibroma to endometriosis must be looked upon as speculative, though not impossible. One does not ordinarily expect endometriosis to be initiated after the menopause, although, rather paradoxically, a ripening follicle is described in the ovary, probably still producing at least some estrogen. As a matter of fact, it is quite certain that the menopause does not bring about a sudden cessation of estrogen production, though the amount of the latter soon becomes insufficient to bring about any bleeding, and after a period which probably varies from a few months to a year or more, estrogen production in the ovary probably ceases altogether. The conditions are the reverse of those seen at puberty. Estrogen production begins several years before the first menstruation, and this is indicated by the fact that breast development and rounding of the girl's figure often precede by many months the first menstrual bleeding.

As regards the relation between the adenofibroma and the endometriosis in the author's case, it must be remembered that the former has its source in the invaginating tendency of the surface epithelium, and it is this celomic tissue which the numerous adherents of the celomic metaplasia theory of the histogenesis of endometriosis believe to be responsible for ovarian endometriosis. When the surface epithelium of the ovary invaginates, even in simple and non-metaplastic form, it undergoes various types of metaplastic change, and among these must be considered an endometrium-like change in the subepithelial stroma. Indeed, a common laboratory diagnostic problem is presented by these uterine gland-like structures, with, but often without, stroma, and usually showing no hemorrhagic tendency. Whether or not to designate them as endometriosis is often a moot point.

Again, in cases of adenofibroma the epithelium often becomes endometrium-like, and in a small proportion of cases it becomes highly proliferative, with not infrequently an acanthomatous tendency like that seen in the ordinary adenocanthoma of the uterus. Such changes as this, while rare, are of ominous significance as indicating potential malignancy, which can conceivably be followed by genuine adenocarcinoma. This may explain some of the not infrequent cases of adenocarcinoma which histologically are so remindful of uterine adenocarcinoma, although it is certain that at least some of these cases have their source in ovarian endometriosis of the common type.

It will thus be seen that the point raised by Hughesdon involves the whole question of the histogenesis of endometriosis, about which we are still far from a complete solution, in spite of the intensive studies of this very common lesion during the 28 years since Sampson established it as a clinical and pathological entity.

Since the writing of the above comment, Dr. Hughesdon has very kindly sent me sections from his case. Whether rightly or wrongly, I did not feel that they established the assumption of endometrial differentiation.—Ed.)

A diagnosis of ovarian cyst was made. At operation a large left ovarian cyst was removed and hysterectomy performed. The pathologic diagnosis was papillary cystadenocarcinoma of both ovaries.

One month after operation, that patient became rapidly worse and was admitted for terminal care. Two hard masses, 4 cm. in diameter, were felt in the right lower quadrant of the abdomen. At this time, testosterone propionate therapy, 100 mg. 3 times a week, was started.

Three months after operation, the patient was discharged from the hospital. She had received 1,200 mg. of testosterone propionate. The patient stated that she had greater energy and a better appetite than at any other time in her life.

Four months after operation the liver was enlarged to 2 fingerbreadths below the costal margin, a hard nodule was felt on the surface. The patient complained of weakness of her voice and loss of hair from her head. The mass in the pelvis was smaller.

Six months after operation (5,600 mg. testosterone propionate given) the mass in the pelvis was barely palpable; another nodule had appeared on the liver. Nine and one half months after operation, the patient died of intestinal obstruction. The total dose of testosterone propionate was 14,100 mg.

At autopsy the liver weighed 3,000 grams and contained multiple massive areas of tumor replacement. The bowel showed no implants except for the region of obstruction in the recto-sigmoid. Metastasis of the primary ovarian lesion was observed in the liver and lungs and lymph nodes.

(The good results of stilbestrol in the palliation of prostatic cancer and the encouraging but definitely less striking benefits of testosterone in some cases of breast cancer have justified continued employment of these methods. This, however, does not mean that we should shoot endocrines into patients suffering with any kind of cancer in any organ. In cases otherwise hopeless, I suppose that there could be no objection to random therapy of this sort. On the other hand, I believe that I would hesitate to report a single case thus treated of a tumor type in which there appears to be no rationale for endocrine therapy, and a type of cancer which exhibits frequent vagaries in its course without any treatment whatsoever. The implication of benefit in such a case might well lead uncritical readers to the probably valueless and conceivably harmful employment of endocrines in all sorts of cancer cases.—Ed.)

ADENOFIBROMA OF OVARY WITH PARTIAL DIFFERENTIATION TO ENDOMETRIOSIS

P. E. HUGHESDON

Proc. Roy. Soc. Med., London, 42: 62, 1949

The patient, 53 years old, single, had a menstrual history of irregular periods with hot flushes 3 years before operation. One year before operation periods stopped. Pelvic examination 16 months prior to operation revealed a mobile mass in the left fornix, interpreted as a slightly enlarged left ovary. Examination before operation revealed a hard craggy mass behind, to the left of and separate

cases radiotherapy is likely to be chosen, but this likewise demands considerable technical skill.

It is to be remembered that at least some of these cases of urethral carcinoma develop in caruncles. Whenever a caruncle, therefore, is in any way suspicious in appearance because of undue vascularity and infiltration, biopsy is of great importance. No such caruncle should be removed by any of the forms of coagulation or fulguration employed by some, as this robs one of the opportunity of making the thorough histological examination possible after surgical excision.—Ed.)

A COMPARATIVE STUDY OF THE EFFICACY OF CERTAIN DRUGS IN PROMOTING EVACUATION OF THE FEMALE BLADDER FOLLOWING GYNECOLOGIC OPERATIONS

C. LINTGEN

Jefferson Medical College Hospital, Philadelphia, Pa.

Am. J. Obst. & Gynec., 56: 1112, (Dec.) 1948

The present study was undertaken in an effort to determine the efficacy of various types of medication designed to decrease the number of catheterizations following gynecologic operations. Five groups of patients were studied. Each one of the first 4 groups of 100 patients was given prostigmine methyl sulfate hypodermically, mercurochrome instillation in the bladder, acriflavine instillation or no medication at all. The fifth group of 21 patients were given "Doryl" hypodermically after operation. Instillation of mercurochrome, 15 cc. of a 0.5 per cent solution, into the bladder at the time of operation was found to be the most effective. The mode of action of this drug and also acriflavine was thought to be due to an irritative action on the mucous membrane of the bladder. Cystometrically, there was little, if any, change in the intracystic pressure before and after the use of mercurochrome and acriflavine; however, there was a slight rise after the use of prostigmine.

(No matter what medication is used, there is an inevitable proportion of patients who are slow in beginning to void spontaneously after gynecologic operations, more particularly those of plastic vaginal type. In the more extensive procedures of this group most of us employ retention catheters for a number of days postoperatively, but not a few patients are unable to void after removal of the catheter, requiring either reinsertion or the institution of regular catheterization. As a part of the management of such cases, the instillation of mercurochrome has, in our experience, often been helpful. The early ambulation which has now become so widely popular has also been of value in promoting the reestablishment of normal voiding.—Ed.)

FEMALE UROLOGY

RADIUM THERAPY IN CARCINOMA OF THE FEMALE URETHRA

ROBERT E. FRICKE AND JAMES T. McMILLAN

Mayo Clinic, Rochester, Minn.

Radiology 52: 533, 1949

A review of the literature reveals that carcinoma of the female urethra is relatively uncommon. The proximal half of the urethra is most frequently the site of carcinoma. The lesions may be polypoid, ulcerative, or infiltrating in gross appearance. There may be extension of the lesion to the anterior vaginal wall; as the disease progresses, the bladder may become involved by direct extension.

Therapeutic measures may be divided into 4 general types: (1) cautery, (2) excision, (3) radium therapy, and (4) roentgen therapy. The smaller the tumor, the more applicable are cautery and excision in the treatment.

The present series includes 35 cases of carcinoma of the female urethra in which treatment with radium was given at the Mayo Clinic from 1918 to 1942. The average age of the patients was 52.4 years. The chief symptoms were dysuria, a mass at the external meatus, frequency and bloody vaginal discharge. Most of the lesions were located in the proximal portion of the urethra; all of the lesions appeared to be infiltrating. Biopsy was performed in 30 cases; of these, 24 were squamous-cell epitheliomas. In 26 of the 35 cases, enlargement of the inguinal lymph nodes was present.

Three methods of applying radium or radon were employed: (1) interstitial implants of radon or interstitial radium needles, (2) contact therapy, and (3) use of a vaginal applicator, radium at a distance of 1 cm. directed at the lesion. Roentgen therapy was used only for the treatment of inguinal nodes or for general irradiation of the pelvis in cases of advanced carcinoma.

Fourteen patients had radium treatment alone, 10 had radium and roentgen therapy, 9 had excision with or without cautery in addition to radium, 2 were treated with excision or cautery and by radium and roentgen therapy. Fifteen (44.1%) patients survived 5 years or more after the diagnosis was made. The best results were obtained in the group of patients who were treated by surgical means and radium. Of the 9 patients in this group, 7 lived 5 years or more. This group consisted of those patients with the earliest and most localized lesions. The poorest results occurred in the group in which radium therapy alone was used; in this group were the most advanced cases. The complications most frequently noted following radium treatment were urethral stricture and incontinence.

(It is fortunate that carcinoma of the urethra is relatively rare, because it is a serious disease, and one offering difficulties in treatment. Surgery offers little and is difficult in all but the earliest cases, the more advanced ones presenting little hope for cure, even when the operative procedure is so extensive as to imply sacrifice of bladder function. In most

OPERATIVE GYNECOLOGY

NOTE ON THE USE OF RADIUM IN CONJUNCTION WITH SURGERY IN GYNABCOLOGY

R. E. TOTTENHAM

Irish J. M. Sc., 278: 125, 1949

The author feels that adenocarcinomas of the body of the uterus is best treated by combining radium therapy and surgery. Radium destroys necrotic fragments of cancer, arrests the growth, and will control hemorrhage during the interval between the diagnostic curettage and the return of the pathological report. If there is no evidence of malignancy, further treatment is unnecessary.

Three cases are cited in which radium very satisfactorily controlled the bleeding between biopsy and operation.

(See comment on following abstract of paper by Hundley et al.—Ed.)

ADENOCARCINOMA OF THE UTERUS: OBSERVATIONS ON TREATMENT AND HISTOLOGIC FINDINGS FOLLOWING INTRACAVITARY RADIATION

J. M. HUNDLEY, E. S. DIGGS AND T. KARDASH

University of Maryland School of Medicine, Baltimore, Md.

Am. J. Obst. & Gynec., 57: 52, (Jan.) 1949

The authors have reviewed the cases of adenocarcinoma of the uterus which have come under their care, with special reference to the 5-year survival rate in the various plans of treatment. The cases have been divided into 2 major groups, determined by the ability of the patient to undertake a specific plan of therapy. The first group, or the good risk patients, were treated first with intrauterine radium in dosages varying between 4000 to 4500 mgm. hours. This was followed in 4 to 6 weeks by a panhysterectomy and a bilateral salpingo-oophorectomy. Approximately 4 to 6 weeks postoperatively, 64 per cent of these patients were given additional deep x-ray therapy and a total of 8000 r was given through multiple portals. The poor risk group, or patients in whom operation was not feasible because of advanced age, severe hypertension, etc., received 4500 mgm. hours of radium and this was followed in 4 to 6 weeks with 8500 r by deep x-ray therapy.

The results in the first group were very satisfactory, with 84 per cent of the 32 patients so treated showing a 5-year survival. The 5-year survival rate of 34

OSTEITIS PUBIS IN A FEMALE FOLLOWING URETEROLITHOTOMY

E. J. MCGINN

Marshfield, Wisconsin

Urol. Cut. Rev., 53: 264, 1949

The author reports the 4th case of osteitis pubis occurring in a woman. The etiology of the disease is obscure. Infection due to retropubic leakage of infected urine is considered an important cause. Trauma may also be a factor. Clinically, the condition simulates infection; roentgenographically, it simulates acute bone atrophy.

The symptoms begin several weeks after operation. Pain usually begins in the region of the symphysis pubis. Sometimes a thickening and widening of the symphysis may be palpated. In most instances, no special therapy outside of bed rest and assurance are needed. Only rarely do abscesses develop that require surgical drainage. Pathologically, the changes induced by this lesion vary from a simple periostitis to an extensive lesion in the bones with necrosis of the cartilage and bone followed by subsequent healing.

The patient was a 55 year old white female who had a ureterolithotomy performed May 10, 1945. She was again seen 2 months after operation complaining of pain over the lower abdomen which radiated into her thighs. Tenderness was elicited over the lower abdomen and symphysis pubis. X-ray and urological examinations were negative. One month later, she returned, stating that she was unable to walk and had constant pain over the symphysis pubis. Examination revealed tenderness over the rami of the pubic bones and thickening of the symphysis pubis on pelvic examination. X-ray showed atrophy of the pubic bones involving the bodies as well as the rami. The patient was kept on bed rest for 20 days with diathermy treatments and penicillin. At the end of this time, she was dismissed asymptomatic. One and one half years later, the patient had a recurrence. There were no urological findings at this time. Bed rest resulted in subsidence of her clinical complaints.

It is the impression of the author that penicillin is of no great value in the treatment of osteitis pubis. The etiological factor in this case is obscure, although the infected urine at the site of ureterostomy must have been a factor.

(The above case should be of interest to those gynecologists who include female urology in their work. The author suggests that the causative factor in the osteitis pubis may be infection from the urine at the time of the ureterolithotomy, but this seems difficult to reconcile with the long latent period in the development of the symptoms, and the fact that recurrences occurred as long as 1½ years later.—Ed.)

ABDOMINAL TOTAL HYSTERECTOMY WITH IMPORTANT
MODIFICATIONS IN TECHNIQUE

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J. Nat. M. A., 41: 65, 1949

Total abdominal hysterectomy is more frequently being chosen because it eliminates the possibility of subsequent stump carcinoma. The latter is reported to occur in anywhere from 2.3 to 6.9% of the cases in which subtotal hysterectomy is performed.

If the cervix is diseased at the time of hysterectomy, the total procedure is to be preferred. If cauterization or conization of the diseased cervix is performed, hysterectomy should be deferred for at least 2 months to complete healing of the cervix and of the parametria.

In properly selected cases total hysterectomy does not require more than 10 to 15 minutes longer than subtotal hysterectomy. However, severe pelvic inflammatory disease, extensive endometriosis, or poor physical condition may contraindicate the total operation. In such cases, the diseased cervix can be electrically conized at the conclusion of the abdominal operation.

At Harlem Hospital in the period from March 1946 to April 1947, abdominal hysterectomy for myoma was performed 282 times. Fifty-four per cent of the operations were total, with no deaths, no infections and no urinary tract injuries. In the 131 subtotal hysterectomies performed, there was one injury of the ureter, 2 bladder injuries, and 2 wound infections.

The author's technique is as follows: for 3 consecutive days preoperatively the vagina is painted with Scott's solution. On the morning of operation a gauze pack soaked in Scott's solution is placed in the vagina. The removal of the uterus is then carried out in a routine manner. The parametria are fixed to the angles of the vaginal vault with #2 chromic catgut. A running lock stitch of #1 chromic catgut is then inserted around the entire vaginal vault, including the endopelvic fascia, the paravesical tissue, and the uterosacral area. The round ligaments and adnexal stump are fixed to the vaginal vault at its lateral angles. The vaginal vault is left wide open.

(Approximately one half of the author's hysterectomies were total and one half subtotal, and it is of interest to note that the complications occurred in the latter group, these including 1 ureter and 2 bladder injuries, and 2 wound infections. This probably proves nothing except the variability of individual reports, due to individual circumstances, especially where the number of reported cases is rather small. In general I do not think there is any doubt that the risk of bladder and ureter injury is somewhat greater in the total operation, and this is unquestionably true with the occasional total vaginal hysterectomy. In the hands of the expert, and especially the one who has sense enough to settle for the subtotal operation in the inevitable minority of cases which look forbidding or unduly hazardous from the total standpoint, the complete operation soon becomes about as simple and safe as the subtotal.

patients in the second group, however, was only 20.6 per cent. In this series there was no operative mortality and no untoward sequelae were noted during convalescence.

The uteri and adnexa of 67 patients treated by irradiation were available for histological study. Nineteen, or 28.5 per cent, of the uteri and adnexa showed no residual malignancy and residual carcinoma was found in 48 cases. Extension of the growth into the myometrium was noted in 31 and was confined to the endometrium in 17 instances. Tubal involvement was found in 4 patients, and the ovary was affected in 3. Uterine myomas were associated with corpus carcinoma in 27 patients.

From this study, the authors concluded that intracavitary radiation by multiple sources, followed by panhysterectomy and bilateral salpingo-oophorectomy is the procedure of choice in the treatment of corpus carcinoma. The histological studies would indicate a relatively high incidence of residual malignancy, and this leads the writers to believe that panhysterectomy is of greatest importance. Although residual carcinoma was found in 71 per cent of the specimens, the vast majority of the residual cells showed some evidence of radiation reaction.

(The chief lesson to be drawn from the authors' report, it seems to me, is the indispensability of panhysterectomy as a part of the treatment of adenocarcinoma of the uterus. This is indicated by the fact that fully 48 of the 67 patients who had been subjected to preliminary irradiation, including both intracavitary radium and Xray, still showed residual carcinoma, in the removed uterus. This incidence is even higher than the approximately 50 per cent reported by most authors. The unusually good results obtained in the patients treated by the combined plan (84 per cent 5 year survivals) as compared to the poor salvage in those treated only by irradiation, even making allowance for the fact that the latter group includes more advanced cases, would lead one to believe that the contraindications for operation should be cut down as much as possible, since the somewhat greater primary operative hazard would probably be more than counterbalanced by the greater salvage prospect of the operative plan.)

In view of the fact that residual carcinoma is found in such a large proportion of the removed uteri, I confess that I find it difficult to understand why the combined plan should give results apparently definitely better than those obtainable from surgery without preliminary radiation. Granted that the hazard of infection is lessened, I do not think that this would have great influence upon primary mortality rates, especially in these days of chemotherapy and antibiotics. Granted also that the fibrosis and the entrapment of residual cancer cells lessen the risk of operative dissemination of cancer cells, I again do not believe that this risk is of appreciable importance if proper precautions are taken at operation, such as closure of the external os by suture, the application of clamps to the broad ligaments at the very outset of the hysterectomy, etc. I know how unorthodox it is to express such doubts at a time when the combined plan is the fashion, but I do not believe that there have as yet been a sufficient number of comparative studies of results with the two plans in clinically comparable clinical stages. My own reaction at present has been not to hesitate to proceed with radical operation without preliminary radiation on early cases, sometimes at the same sitting as the diagnostic curettage, when immediate naked-eye or microscopic diagnosis is possible, as it not infrequently is. On the other hand, in the more advanced cases, especially where there is marked enlargement of the uterus, I employ preliminary radiation, as this has appeared to me to make the subsequent operation easier and safer. It seems to me that this question is still to be looked upon as one of the many in the field of cancer therapy which must be regarded as *sub judice*. Other considerations, like the psychological effect upon patients by the combined plan, have not been touched upon in this comment, but they are not unimportant.—Ed.)

In 1930, Bonney reported 284 cases on the 5-year basis, with an operative mortality of 16.5% and a cure rate around 40%; and 181 cases on the 10-year basis with a cure rate around 36%. There are 2 methods of assessing the number of cures. In the first method, all patients lost sight of or dying of other disease are reckoned as having died of carcinoma; in the second method, these cases are excluded from the calculation. In all communications on the subject, the author has given both estimates.

In 1935, the author reported 384 cases on the 5-year basis with a cure rate of 39% or 41%, according to the method of calculation; 283 cases on the 10-year basis with a cure rate of 29% or 33%. At this time, the author emphasized the fact that a large number of the stage III cases could be successfully operated upon.

In 1941, Bonney reported 500 operations on the 5-year basis with a cure rate of 40% or 43% and an operative death rate of 14%. For 415 cases on the 10-year basis, the cure rate was 31% or 36%, according to the manner of computation, and the operative mortality slightly less than 14%. Of the 500 operations, 300 of the patients were gland-free, and 200 gland-involved. Of the gland-free group on the 5-year basis, 53% or 58% were cures; on the 10-year basis, 42% or 49% were cured. In the gland-involved group, 22% or 23% were cured on the 5-year basis; and 16% or 18% were cured on the 10-year basis. The operative mortality in the gland-free group was 10% and that of the gland-involved group was 20%. It may be said that gland-involvement doubles the risk of operative death, and more than halves the average chance of cure.

The absolute operative achievement is the number cured out of every 100 unselected patients seen. Reckoning his operability-rate as 63%, the author's achievement was 25% or 26% on the 5-year basis, and 20% or 21% on the 10-year basis. Surgery can effect one 5-year cure out of every 4 unselected patients, and one 10-year cure out of every 5 unselected patients.

The 5-year cure rate for all cases has been around 40%, and the 10-year cure rate has been around 35%. The author has not varied his standard of case selection or his technique in material details over 29 years. The operative mortality was 20% in the first 100 cases, 14% in the next 200 cases, and 11% in the last 200 cases. Most of the operative deaths followed operations on patients with very advanced disease, only a few of whom would have figured as cures.

The figures given above related to patients operated on before the existence of the accessories, adjuncts and aids which surgeons now enjoy. They are the results of pure surgery; no irradiation was used either before or after the operations except in a very few cases.

There is much evidence of recent years that pre-operative irradiation is helpful. The truth of the matter is that in certain cases surgery, and in others radium, would give the best chance of cure. The author deprecates as altogether premature the appeals which have been made to the younger gynecological surgeons not to embark on the operative treatment of cancer of the cervix, but instead to take up radium therapy. Until the specific cure for cancer has been found, surgery and radiotherapy alike are make-shifts—a humbling thought and one which should discourage the acrimony which has crept into their rival claims.

The 3 days' preliminary disinfection of the vagina seems unnecessarily elaborate, most surgeons considering immediately preoperative disinfection as adequate protection. I like the author's technique of running a lockstitch around the vaginal edge, probably because I have long used it myself. Too many operators do not appreciate the vascularity of the vaginal mucosa and the hazard of postoperative bleeding if one depends only on a few interrupted or figure-of-eight sutures.—Ed.)

WERTHEIM'S OPERATION IN RETROSPECT

VICTOR BONNEY

Lancet, Lond., 1: 637, 1949

In 1905, Professor Wertheim described the operation which now goes by his name. He claimed 40 five-year cures out of every 100 patients operated upon, as against 10 or less obtained by simple abdominal or vaginal total hysterectomy. He asserted that his operation was applicable to 50% of all cases of carcinoma of the cervix. In the first 100 operations that Wertheim performed, there were 30 deaths.

With the illustrations in Wertheim's article as a guide, the author performed his first successful operation in 1907. In 1913 Berkeley and Bonney reported 71 operations on a 3-year cure basis, with an operative mortality of 22% and an operability rate of 63%. The operability rate in the author's private patients, seen between 1910 and 1929, was 80%.

The author's technique departed somewhat from that of Wertheim; the regional glands were removed routinely, whereas Wertheim did not touch them unless they were obviously involved. Further, instead of removing only sufficient vagina to form a cap over the cervix, the author removed the whole of it and replaced the vaginal clamps used by Wertheim with his own instrument.

In 1916, Berkeley and Bonney published a series of 100 cases. The operative mortality was 20%, and 39 of the patients were well 5 years after operation. At this time, the cases were classified according to whether the regional glands were or were not carcinomatous. This classification proved useful in proving that a proportion of the cases whose glands are involved can be saved by surgery.

In 1921, Bonney reported his first 100 operations. There were 20 deaths, 40 survivals for 5 years and an operative 5-year achievement of 25%. In 1925, 192 operations had been performed with a mortality of 16%.

In 1929, the author reported 265 cases on the 5-year basis with 40% cures, and 161 cases on the 10-year basis with 36% cures. Ten per cent of all recurrences occur between the 5th and 10th years; 10 years' survival is 100% cure.

Comparison of radiological and surgical treatment is valid only when pure radiology is compared to pure surgery. The division of carcinoma of the cervix into stages is misleading: for the pre-operative diagnosis is often found to be wrong when the abdomen is opened. All that matters is the number of patients seen, the number treated, and the number of 5-year and 10-year survivals.

STERILITY

CERVICAL OBTURATION WITH INFLATABLE CANNULA IN UTERO-TUBAL INSUFFLATION AND HYSTEOSALPINGOGRAPHY

I. C. RUBIN AND E. MYLLER

New York, N. Y.

Am. J. Obst. & Gynec., 56: 1077, (Dec.) 1948.

Cervical obturation during uterotubal insufflation and hysterosalpingography is essential to prevent escape of air or CO₂ and the consequent loss of pressure. The use of the metal or rubber acorn may prove unsatisfactory if the cervix is irregular, and the pressure applied against such an obturator to hold it in place may kink or distort the tubes. The ideal uterine cannula should have the following characteristics: its application should be painless and unaccompanied by trauma; it must provide air-tight obturation of the cervical canal; and it should maintain the normal anatomical position of the uterus.

The authors have described a cannula which they have employed with satisfactory results. The cannula has a double barrel, one of which opens on the end and the other on the side. A rubber balloon covers the side opening. The cannula is inserted into the cervical canal and the balloon is distended with 1 to 3 cc. of water, depending on the size of the cervix. The contrast medium or gas is then injected through the other barrel and a manometer can be attached to the proximal end of the cannula. The instrument holds its position without altering the anatomy of the uterus and can be inserted without trauma to the cervix.

(Every gynecologist must often have been annoyed by the fact that no matter how snugly the acorn type of the cervical obturator ordinarily employed in the performance of tubal insufflation may be fitted into the canal, the gas may still leak out from the latter. Increasing the pressure on the acorn with the "fork" which fits into its circular groove, or changing the angle of this pressure, will usually get rid of the leak, but often at the cost of considerable time and irritation. Certain types of metallic obturators of spiral or corkscrew type are used by some, while others think them too traumatizing to the endocervix. The new inflatable cannula described by the father of tubal insufflation, Rubin, in collaboration with Myller, sounds as if it might be the answer to the problem, if it proves to be as easy of manipulation as the description suggests. It would seem to me that the new device might be resorted to only in the minority of cases in which the ordinary type of cervical plug is unsatisfactory in preventing leakage.—Ed.)

(The author of this paper has played a distinguished part in the fight against cancer, and on the surgical front the contribution of Victor Bonney is no less important than that of Wertheim. No one interested in the surgical aspects of cervical cancer can afford not to read the present paper, if for no other reason than that it gives such an excellent historical review of the early days of operation for this disease, as well as an authentic personal account of Bonney's own accomplishments. Before the introduction of radiotherapy, as well as throughout that long phase when the latter was the almost universal method of treatment, Bonney remained the world's leading exponent of the surgical plan.

Those who read his paper may be surprised to learn that even from the beginning the operation done by Bonney was much more extensive than that recommended by Wertheim. The latter, for example, did not routinely perform gland excision, as many American gynecologists seem to believe. Bonney, on the other hand, has always stressed the importance of this step, and the figures he reports would seem to attest its value, in the hands of the expert operator. The criticism most frequently made of Bonney's surgical plan was the high primary mortality, which was not surprising in view of the fact that most of his cases were operated upon before the general use of such surgical adjuncts as transfusion, antibiotics and chemotherapy. It will be noted, however, that as his series stretched over the years, there was a steady decline in the primary death rate.

The author properly criticizes the frequent inaccuracy of clinical stage classification. *The surgeon, unlike the radiologist, has frequent opportunity to observe that the pre-operative classification must be changed by the findings at operation, although I do not believe that surgeons as well as radiologists would generally be inclined to discount clinical classification as completely as does Bonney, even though they appreciate its limitations.*

The cure rates reported by Bonney are equalled or excelled by many of those reported by modern radiologists, and one may wonder why there should have been such a revival of the surgical plan in recent years, in spite of the very low primary mortality rate reported by most authors. Certainly the operations now done by most of the surgical exponents are not any more radical than that of Bonney, and there is no doubt that in the hands of many operators, they are less extensive and less expertly done. There are as yet no worthwhile 5 year reports of the newly revived surgical plan, but if, when available, they show any strikingly better results than those of Bonney, aside from the improvement attributed to the lessened primary mortality, one might find it difficult to explain them. Such a long time is necessary for the evaluation of any plan of cancer therapy, and the statistics are so bewildering, often puzzling and frequently contradictory, that the whole problem is now fluid and confused. A few clinics appear to have gone "all out" for the surgical plan of attack, this including even far advanced cases usually looked upon as practically hopeless, as witnessed by the Brunswick "all-American" operation of pelvic evisceration.

From my own standpoint, the real punch line in Bonney's paper is contained in the last three lines of the abstract, and I would commend these to the attention of both surgeons and radiologists.—Ed.)

of gynecologic patients, I have been impressed with the frequency with which appendectomy and right salpingo-oophorectomy have been previously done by general surgeons. There is no doubt that in many of these, because of right lower quadrant pain, the patient had had an appendectomy; the surgeon had found an appendix so innocent-looking that he was doubtful of its complicity in the symptoms; and that he had therefore thought it best to fire a double-barreled gun by also removing what was probably an innocent "cystic" right ovary. In many of these cases the seat of the trouble was elsewhere, as in the right ureter. This is only one illustration of the penalties imposed upon patients by looseness and lack of thoroughness in diagnostic studies, and a good many others are discussed by the author of the above paper.

As regards backaches, the author's figures indicate the correctness of the statement that the cause of backache in women is generally in the back itself, and only infrequently in the pelvic organs. The gynecologist must therefore be a sort of amateur orthopedist himself, just as he must know something of psychosomatics. On the other hand, he will wish in many cases to have the benefit of the advice and assistance of the trained orthopedist or psychiatrist.

The general problem of pain perception and its frequent transference and proper interpretation is a complex one. The author obviously is inclined to accept the so-called Head hypothesis in the explanation of visceral pain, and many others still do, though some question has been raised as to its correctness. According to Henry Head, a distinguished British neurologist, the viscera themselves are insensitive to pain. This will not be surprising to those who have had the opportunity of removing abdominal organs or tissues under local anesthesia. An appendix, for example, can be cut or burned with no pain whatever, so long as no traction is made on the mesentery, this being transmitted to the parietal peritoneum, which is highly sensitive. According to Head, the pain of appendicitis is not perceived in the appendix itself, but in the somatic nerves linked up with the same segment as the sympathetic nerve supply of the appendix. My recollection is that the mechanism was explained by Head as similar to that of the neurological phenomenon spoken of as *allochiria*. If, for example, an individual suffers a neurological disease which makes one foot completely insensitive to pain, and if a hot iron is applied to this foot, severe pain is felt in the normal other foot, that is, in the nerves linked up with the same spinal segment as the insensitive nerves of the diseased foot.

While modifications of Head's hypothesis have been urged, it undoubtedly has to be reckoned with in problems of visceral pain and also, as Guerriero says, in the interpretation of areas of cutaneous sensibility. Finally, the psyche which injects itself into such subjective symptoms as pain makes it necessary to be on our constant guard against those psychosomatic factors which color many clinical histories.—Ed.)

PSEUDOHERMAPHRODITISM IN TWINS. REPORT OF THE TENTH CASE

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Am. J. Dis. Child., 76: 208, 1948.

Pseudohermaphrodites are classified as follows: (1) the male type, in which the external characteristics of the male predominate, and (2) the female type, in which the external characteristics of the female predominate. The majority of

GYNECIC SYMPTOM COMPLEXES

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New Orleans M. & S. J., 101: 502, 1949.

In examination of 1,197 patients with complaints relative to disease of their female genitalia, other disease entities were found to cause their gynecic symptom complexes in 506, or 42%. To explain this, the author reviews the basic anatomy and physiology of the nervous pathways of the pelvic viscera.

Interpretation of pain demands consideration of its severity, duration, location and quality. Pain which arises in superficial somatic structures can be evaluated as to these characteristics. Cutaneous pain is of the same quality, no matter what the etiology. Muscle pain is fluctuating and difficult to localize. Visceral pain may be direct or referred.

The pelvic organs remain relatively insensitive to pain; much of the sensation of pain from visceral entities is due to the somatic pain produced by stretching. In cases of so-called uterine or ovarian pain, the etiology may be psychosomatic.

Disease of the urethra, bladder, ureters, and kidneys produces symptoms which are indistinguishable from gynecologic disease. Frequently urologic disease is exaggerated at menses to focus the patient's attention to it. In 44% of the patients who had gynecic symptom complexes, there was proven urologic disease. Of these cases, 20 had been advised that pelvic surgery was necessary.

Backache is usually considered by women as being a symptom of gynecologic disease. Very few gynecologists consider low backache a gynecologic complaint. Backache was noted as a complaint in 220 cases. Orthopedic examination revealed the following etiologic causes: postural (64%), mechanical (27%), infection (8.1%), and new growths (0.9%).

In 60 cases, rectal and sigmoid entities were found to be the etiology of such pelvic complaints as pain, dyspareunia, dysmenorrhea and bleeding. It is not unusual to find carcinoma of the rectum considered as tubal or ovarian disease. The etiologic causes of the symptom complexes in these patients were as follows: colitis (67%), diverticulitis (13%), amoebiasis (8%), carcinoma of the bowel (5%), and polyps of the bowel (7%).

The most important phase of a gynecologic survey in any patient is a thorough history and physical examination with particular emphasis on the genitourinary, the gastrointestinal, and neuromuscular systems. From these systems come the entities that produce gynecic symptom complexes.

(The purpose of this paper is a very salutary one, and the admonitions it expresses should be taken to heart not only by gynecologists, but also by the general surgeons who in so many communities do such a large proportion of the gynecologic surgery. In taking histories

which the external genitals are dominantly feminine and the psychology also of feminine type. A number of such cases have been reported, including one of my own. The desirability of avoiding castration in such cases has been emphasized by Gruenwald in a very recent paper (Gruenwald P., *Am. J. Obst. & Gynec.* 55: July, 1949). It is of interest to note that in a number of cases of this group in which the testes were removed, the patient suffered typical menopausal vasomotor symptoms.

The most important point to stress in the matter of management, it seems to me, is that an individual should not of necessity be assigned to his genetic sex. In the cases of masculine pseudohermaphroditism, for example, it is often easy to amputate a hypertrophied phallus and to construct an artificial vagina. On the other hand, to try to adapt the external apparatus to the male type is often extremely difficult. Attempts to correct a complete hypospadias involve multiple operations, with often a very dubious final result, rarely leaving an organ which would be of much value for male coital purposes. In general, it is much easier to remove redundant organs or tissues than it is to try to build them up if they are lacking. Unorthodox though it may seem, I believe I would not hesitate to consign some patients to a female role even if I knew that the only gonads present were testes. I have done just this in at least one case and I am sure that the same plan has been followed by others. Nothing would be more tragic, or more calculated to produce violent psychic upheaval, than to try to transfer to a male role a patient who has been raised as a girl, and who has the typical feminine psychology which many of these patients have, including libido toward the male.

Within the last few days I have seen a supposedly female infant only a few months old in whom, not at birth but only a few weeks ago, the mother noticed an external genital abnormality, chiefly in the form of a phallic organ measuring 2 cm in length. Four physicians have been consulted, two deciding that the infant is female and two being emphatic that little Charlotte is a male. On examination I feel sure that the phallus is a penis with a complete hypospadias of the urethra. A biopsy of the gonads has not yet been done, but it is planned, since external genital organs of the intersexual glands here present can be found in association with either undescended testes or ovaries. Even if they prove to be testes, I believe that I shall be inclined to vote for a female role for this infant for such reasons as I have mentioned above. I hope that an opportunity will present itself to report to readers of the Survey, on the later findings and developments in this infant when such information is available.—Ed.)

THE ADOLESCENT GIRL

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Practitioner, Lond., 162: 269, 1949.

Adolescence in the female begins about the 12th year; its onset is marked by the menarche. The development of the individual may take 10 years or more to be complete.

The adolescent withdraws into isolation and self-consciousness. This is followed by reintegration and emergence into a human being of civilized type. Modesty, associated with the development of secondary sex characteristics; and disintegration of the personality, associated with the sexual instinct, cause violent

cases are of the pseudo type in which the external sexual parts are mixed but in whom the gonads of only one sex are present.

The author reports the 10th case of pseudohermaphroditism in twins. The mother was a 19 year old white primigravida with a family history of mental defectiveness. Her occupation was selling tickets for a circus sideshow hermaphrodite. Female, premature, identical twins were delivered 8 weeks prior to term. In each twin, the clitoris was enlarged, being 23 x 10 mm. The labia majora were 60% of normal size; a third lip of vaginal mucous membrane circled the vagina as a cuff; a tiny vagina, 1.3 cm. long (not as large as in infants of corresponding weight) was present. The clitoris was covered by mucous membrane on the under side. It appeared that a mere fusion along the lower portion of the clitoris would produce a penis. The infants were classified as monozygotic female pseudohermaphrodites of the external type.

McCullaugh (Tice's Practice of Medicine, 1927) felt that although the immediate factor in determination of sex is the gene, the degree of sexual differentiation is determined by hormonal influence. Endocrine imbalance, either in the mother or in the embryo, may produce congenital pseudohermaphroditism.

Operation, or other procedures to determine sex, is desirable as early as possible. Pre-pubertal classification of the proper sex of the individual gives a much better chance for final sexual adjustment. The hermaphrodite assumes the sexual rôle that is in accordance primarily, not with his somatic characteristics, but with his feminine or masculine up-bringing.

(I hope that there was nothing wishful in the fact that a woman whose job was that of exhibiting a hermaphrodite should add to her stock in business by producing 2 of her own. A familial tendency to pseudohermaphroditism has been shown in a good many cases, and it may surprise some that the author was able to find only 9 previous cases in twins. The author describes the clitoris in his case as covered by mucous membrane on the under side, and one wonders whether this could have been a phallus with the complete hypospadias so often seen in pseudohermaphrodites. As a matter of fact, it is often impossible to be sure of the genetic or gonadal sex of the individual without doing a biopsy of the sex glands, as identically the same intersexual appearance of the external genitals may be seen in individuals with either testes or ovaries, or, for that matter, both.

In the examination of the external genitals, one must remember that a male phallus with a complete hypospadias may simulate a large clitoris, that a cleft scrotum may resemble labia majora, and that what looks like a tiny vaginal orifice may be the urethra or a combined urethra and extremely rudimentary vaginal canal. For this and other reasons, it is surprising to read the statement in the author's first paragraph to the effect that classification of pseudohermaphrodites is on the basis of predominance of external genital characteristics. The prevailing method of classification is that of Klebs, based on the masculine or feminine character of the sex glands, the primary masculine and feminine groups being subdivided into an external and internal depending on whether the external or internal end organs of sex show departures from the normal, with a combined form when both the external and internal genitalia are involved. For example, if, as does not appear from the abstract, the ovarian histology of the gonads was established by biopsy, his case would be classified as one of pseudohermaphroditismus femininus externus. Incidentally, sex hormone studies have been found to be of no particular importance in differentiating the sex of such individuals, as one and the same gonad is capable of producing both male and female sex hormones. This is of considerable practical importance, emphasizing the importance, for example, of not removing the testes in the cases of pseudohermaphroditism in

AUTHOR INDEX

OCTOBER, 1949

- Angrist, A., 660
 Arnold, W. T., 686
 Assali, N. S., 605
 Atkins, H. J. B., 683
 Bacon, W. B., 706
 Barber, A., 659
 Bartley, M. D., 643
 Baxter, J., 665
 Bayle, M. A., 715
 Beacham, D. W., 642
 Beacham, H. T., 642
 Beacham, W. D., 642
 Belt, E., 692
 Bolton, J. P., 712
 Bonney, V., 726
 Brooks, E. F. J., 673
 Brunschwig, A., 699, 702
 Campbell, W. R., 676
 Chapman, J. C. F., 695
 Christie, A., 661
 Collier, T. W., 731
 Cordes, F. C., 659
 Cutbush, M., 653
 Cuyler, W. K., 698
 Danforth, D. N., 695
 Davis, G. H., 703
 Delson, B., 710
 de Santiago, A. P., 682
 Detweiler, H. K., 674
 Deweese, W. J., 713
 Diggs, E. S., 723
 Donnelly, J. F., 634
 Drell, M. J., 637
 Ellis, H. B., 664
 Feeney, J. K., 669
 Fournier, J. C. M., 682
 Frantz, M. J., 681
 French, W. G., 703
 Fricke, R. E., 720
 Gandek, C., 643
 Gellis, S. S., 662
 Greenblatt, R. B., 705
 Greene, R. R., 715
 Greentree, L. B., 687
 Guerriero, W. F., 730
 Hawkins, T. F., 631
 Hertz, R., 701
 Hesseltine, H. C., 678
 Hill, L. M., 633
 Howe, J. S., 703
 Huffman, J. W., 704
 Hughesdon, P. E., 718
 Hundley, J. M., 723
 Hurxthal, L. M., 686
 Israel, S. L., 689
 Jarcho, J., 625, 628
 Javert, C. T., 624
 Johnson, A. B., 667
 Jones, G. E. S., 679
 Kardash, T., 723
 Kernodle, J. R., 698
 Kirschbaum, A., 681
 Kirchhoff, H., 647
 Kraus, A. P., 641
 Kron, W., 691
 Lash, J. J., 692
 Lawlor, M. K., 632
 Levy, S., 655
 Lintgen, C., 721
 Lisa, J. R., 691
 Loeb, L., 711
 Logan, M. A., 633
 Lubin, S., 710
 McCall, M. L., 668
 McGanity, W. J., 639
 McGinn, E. J., 722
 MacGregor, A. R., 654
 McHenry, E. W., 639
 McLane, C. M., 692
 McMillan, J. T., 720
 Mauzy, C. H., 634
 Menk, K. F., 716
 Meyerhardt, M. H., 644
 Mollison, P. L., 653
 Moss, J. M., 716

emotional conflicts. Reintegration, frequently associated with identification with an older woman, culminates in an adult type of adjustment to society.

It is essential that the mother-father relationship be in good repair at the time of adolescence of the daughter. Excessive regard between the father and daughter should be avoided. It is important that the girl should have interests outside the home.

Sex education should be begun in early childhood. The general mechanism of menstruation should be understood before the menarche. The false sexual values propagated by the cinema should be combated by youth centers, playing fields and clubs.

Psychogenic disorders are frequent in adolescent girls because of conflicting urges. Amenorrhea, enuresis, anorexia, acne, asthma, vasomotor instability, and abnormal behavior patterns may be noted.

Parental anxiety should be alleviated by reassurance from the family physician. At this stage, the girl needs freedom rather than security, encouragement rather than threats or warnings.

(This paper is evidently written by a psychiatrist rather than a gynecologist. This statement is not meant to be derogatory, but I have the feeling that psychiatrists are inclined to accent more strongly than gynecologists the emotional conflicts of adolescence. That these upsets can occur is undoubted, but as a rule they are of minor degree and transitory. Like other psychic influences of early life, however, they may exert a considerable influence on the individual's later life and psychic make-up, and the author does well to call attention to these possibilities. Even more than with the functional disorders of menstruation so often seen in adolescents such as amenorrhea and dysmenorrhea, education and reassurance of the mother is sometimes more important than treatment of the girl herself. Often the mother has many wrong ideas as to the significance and possible harmfulness of these functional disorders, and just as often she may become unduly apprehensive concerning the personality changes which develop in a good many adolescent girls, such as increased shyness and self-consciousness, and perhaps a tendency to withdraw herself, day-dreaming and morbidity. It is the mother who can best guide the daughter through this transitory phase, but she is often inadequately equipped for this purpose unless she in turn is properly guided by the doctor.—Ed.)

Review

PREGNANCY AND LABOR COMPLICATED BY PELVIC ECTOPIC KIDNEY ANOMALIES

A REVIEW OF THE LITERATURE

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Dystocia due to anomalies and tumors of the pelvis and soft parts of the birth canal has been thoroughly discussed in most modern treatises on obstetrics. In the group of tumors including fibromyomas and ovarian cysts which may block the birth canal, ectopic pelvic kidney is casually mentioned as an additional cause of obstruction to normal delivery. Most of the popular American obstetrical textbooks quote references on this subject extending back to the turn of the twentieth century using the papers of Cragin (14) and Bland Sutton (20) written in 1898 and 1901 respectively. Because of the lack of recent information on this subject and our recent experience with several cases, a survey of the literature was made. In order to refresh the obstetrician's memory a few general remarks on the embryology and anatomy of ectopic pelvic kidney will also be reviewed.

EMBRYOLOGY AND ANATOMY OF ECTOPIC, HORSESHOE, AND MOVABLE KIDNEYS

Early in embryonic life according to Pohlman (71) the ureteral buds are formed from the posterior aspect of the Wolffian ducts (5 mm. human embryo). These blind ends form contact with masses of nephrogenic tissue lying in the pelvis. During the process of growth and division of the ureteral anlage, the kidney ascends from its position in the pelvis, reaching the renal fossa by the eighth week of embryonic life. This ascent continues throughout fetal life and even at birth the lower renal poles may be in the iliac fossae. During its ascent the developing kidney receives its blood supply in several temporary stages from large vessels situated in the adjacent vicinity. As ascent continues, the temporary vessels degenerate until permanent renal arteries and veins are established.

Thus it is possible for the developing kidney to be arrested low in the lumbar region, near the promontory of the sacrum, overlying the iliac vessels, or in the true pelvis itself. Renal ectopia may be bilateral and of different degree on the two sides. The kidneys may remain separate, or they may fuse across the midline, forming the so-called horseshoe kidney. Most ectopic kidneys remain on their own side of the body but a few lie in the midline or on the same side as the normal kidney, producing the entity known as crossed renal ectopia. In the latter, the two kidneys are usually fused but occasionally they are separate. Since the normal kidney frequently extends below the iliac crest, only those

Murray, P. M., 725

Myller, E., 729

Oliver, E. B., 671

Owens, E. U., 656

Owens, W. C., 656

Papanicolaou, G. N., 697

Perlin, I. A., 695

Perlow, S., 641

Perry, H. A., 655

Pfeiffer, C. A., 684

Pierce, V., 702

Potter, E. L., 650

Prigot, A., 633

Reid, D. E., 646

Reynolds, S. R. M., 710

Rhaney, K., 654

Ricci, J. V., 691

Rohn, R. J., 643

Rosenberg, B., 638

Rosenbluth, M. B., 638

Rosenthal, A. E., 638

Rubin, I. C., 729

Rushforth, W., 733

Rykert, H. E., 672

St. John, B. D., 717

Sanders, M., 633

Sayre, G. P., 693

Shettles, L. B., 614

Simmons, J. M., Jr., 664

Singer, K., 641

Speert, H., 700

Stillman, N., 660

Stokes, A. B., 675

Suran, R. R., 705

Tauber, R., 709

TeLinde, R. W., 679

Thom, C. H., Jr., 691

Thomas, W. L., 698

Tottenham, R. E., 723

Van Wyck, H. B., 639, 674

Watt, G. L., 639

Weidenbusch, A., 649

Word, B., 671

Wright, L. T., 633

Yudkin, S., 662

ous. The artery or arteries supplying an ectopic kidney arise from an adjacent part of the aorta or from one of the iliac arteries. Usually more than one artery supplies the kidney.

A certain degree of mobility is found in all normal human kidneys. During respiration the kidney may have an excursion of 2-5 cm. Descent of the kidney beyond 5 cm. is referred to as movable or floating kidney, or nephroptosis. Hinman (74) states that movable kidney occurs in 20% of women and 2% of men, most frequently between 20-40 years of age. Lax abdominal muscles following pregnancy, surgical operations, asthenia, narrow flat chest with downward displacement of thoracic organs, weakness of perirenal fascia are listed as the primary causes of movable kidney. Since very few cases of movable kidney have obstructed pregnancy or labor, only slight mention of its anatomy will be made.

TABLE I
Incidence of Pelvic Ectopic Kidney (Males and Females)

AUTHOR	MATERIAL	INCIDENCE
Thompson (1914)	1 case: 13,505 autopsies	1:13,505
Stewart-Lodge (1923)	3 cases: 6,500 autopsies	1:2,166
Shore (1930)	1 case: 1,464 autopsies	1:1,464
Thomas-Barton (1936)	7 cases: 22,000 autopsies	1:3,142
Thompson-Pace (1937)	3 cases: 11,000 autopsies	1:3,666

TABLE II
Incidence of Horseshoe Kidney (General Population)

AUTHOR	MATERIAL	INCIDENCE
Botez (1912)	72 cases: 51,504 autopsies	1:715
Guizzetti-Pariset (1911)	31 cases: 20,000 autopsies	1:645
Gutierrez (1934)	Urological cases	1:400
Bell (1946)	94 cases: 35,329 autopsies	1:376

Horseshoe kidneys are produced embryologically as a result of fusion of the renal blastemas, occurring in the eighth to tenth week of fetal life. Usually fusion of the lower poles takes place across the median line. Beyer (75) collected 18 cases in which the upper pole was fused; but in 94 cases of horseshoe kidney studied by Bell (76) all of the cases were fused at the lower poles. The number of cases which extend into the pelvis is difficult to determine. Most of the cases reported have the isthmus at the level of the bifurcation of the aorta. In this position the renal mass is too high to cause dystocia. A few cases including one of the present study extended into the pelvis.

The incidence of these developmental anomalies of the kidney in the general population are shown in Tables I and II.

REVIEW OF THE LITERATURE

The subject of ectopic pelvic kidney in males and non-pregnant females is very well reviewed by Bell (76), and Everett (77). Papers by Thompson and Pace (58), Thomas and Barton (78) are also of value. Horseshoe kidney has been

kidneys that lie mainly or entirely below the iliac crest should be considered as ectopic. The designation abdominal, iliac or pelvic is also used in describing ectopic kidneys.

Eisendrath and Rolnick (97) have advanced an anatomical classification of renal ectopia which is as follows:

1. Lumbar renal ectopia
 - a. High—when the kidney is above the second lumbar vertebra
 - b. Low—when kidney is between the iliac crest and third lumbar vertebra
 - c. Iliolumbar—if the kidney lies over the crest of the ilium
2. Iliac renal ectopia—when kidney lies in iliac fossa
3. Iliopelvic renal ectopia—when kidney is at level of the brim of the true pelvis
4. Pelvic renal ectopia—the kidney lies in the true pelvis either over the sacral promontory, in the concavity of the sacrum, or on the pelvic floor

The true pelvic ectopic kidney, therefore, lies in the posterior pelvic wall often in a median position in the hollow of the sacrum.

It is possible to distinguish iliac and pelvic kidneys by their position. Moreover, kidneys in the true pelvis usually show gross deformities since their shape is altered by adjacent organs and they lack a fatty capsule. Occasionally the ectopic kidney is hypoplastic, and sometimes it is a solitary pelvic kidney. Fortunately for the obstetrician, solitary pelvic kidney will be encountered in only a few instances. Stevens (98) in 1937 pointed out that solitary kidneys occur in 1:1000 people but that pelvic kidneys occurred only once in every 22,000 persons. Stevens' (98) report which included 25 cases of the literature and two cases of his own was supplemented in 1942 by McCrea (72) who discussed 35 cases. Of these, 14 were females and all but one showed malformed genitalia. Nine had absence of the vagina. Rudimentary vagina occurred once, absent uterus 4 times, and absent or misplaced adnexa 7 times. L. R. Wharton (99) has recently reviewed the problem of congenital malformations associated with developmental defects of the female reproductive organs. He particularly emphasizes the importance of a urological-obstetrical consciousness regarding the frequent association of kidney anomalies and genital defects.

Lowsley and Menning (100) in 1944 reported an additional case of pelvic single kidney and increased the case total to 36. These authors found a high mortality in pelvic single kidney. Of 13 cases operated upon, 4 (30%) died: in 25 cases diagnosed during life, 3 (12%) died of renal failure. Hanley and Steel (73) in 1947 increased the number of solitary ectopic kidneys to 44 cases.

Bilateral renal ectopia does not occur very frequently in the general population or in pregnant women. P. E. McCown (46) in 1929 collected 24 cases of bilateral renal ectopia with 2 of his own to make a total of 26 cases. Of these, 12 had pelvic bilateral renal ectopia and of the 26 cases reviewed, 12 were males and 11 were females; in 3 cases the sex was not given.

As early as 1898 Cragin (14) differentiated movable or "floating" kidney from congenital pelvic kidney with the three following criteria: 1) Mobility of the kidney, 2) Length of the ureter, 3) Arrangement of blood vessels. In a true ectopic kidney, the ureter must be shorter than normal, often dilated and tortu-

In Table III, 98 cases of pregnancy and labor complicated by pelvic ectopic kidney anomalies from 1828 through the year 1948 in the previous literature are recorded. These 98 cases were contained in 70 different reports. With the exception of Thompson and Pace (58), no authors have reported more than one, two, and in a few instances 3 cases of this entity. Thompson and Pace mentioned only casually the obstetrical significance of their 21 cases since they were primarily concerned with the subject of ectopic kidney in both male and female patients from a urologic and not necessarily from an obstetric point of view.

Certain essential facts may be garnered from Table III of which the maternal and fetal mortality figures are most important and may be summarized as follows:

Years 1882-1948

Number of mothers.....	98
Number of maternal deaths.....	10 (10.2%)
Total number of pregnancies in 98 mothers.....	226
Total number of abortions.....	35 (15.4%)
Number of premature infants.....	9 (3.9%)
Deaths of premature infants.....	4 (44.4%)
Number of full term infants.....	182
Deaths of full term infants.....	28 (15.3%)
Deaths of viable infants.....	32 (16.7%)
Total fetal loss in 226 pregnancies (including abortions).....	67 (29.6%)

From the above tabulation the outstanding data are the 10 maternal deaths or a 10.2% maternal mortality for 98 mothers. Closer analyses of the deaths in the literature are listed in Table IV. No maternal death from pelvic kidney anomalies has occurred since 1927, when a solitary kidney was removed at the time of cesarean section. Of the 10 deaths, 3 were from shock, 2 from infection, one each from eclampsia, ruptured uterus, and acute hemorrhagic nephritis. Two deaths were due to ill advised procedures with the entity of solitary kidney. In one case the entire kidney function of the patient was removed at the time of cesarean section. In a second case, partial nephrectomy was performed in an attempt to preserve some kidney cortex from infection without beneficial result. Since most of the deaths occurred before 1927 it seemed apparent that the 10% maternal mortality would be misleading in the light of present day obstetrical knowledge. For this reason an arbitrary twenty year period from 1928 to 1948 was selected for tabulation. A more recent idea of the fetal mortality associated with pelvic ectopic kidney anomalies may thus be gained.

Years 1928-1948

Number of mothers.....	48
Number of maternal deaths.....	0 (0%)
Total number of pregnancies in 48 mothers.....	79
Total number of abortions.....	11 (13.9%)
Number of premature infants.....	5 (6.3%)
Deaths of premature infants.....	2 (40%)
Number of full term infants.....	63
Deaths of full term infants.....	8 (12.6%)
Deaths of viable infants.....	10 (14.7%)
Total fetal loss in 79 pregnancies.....	21 (26.5%)

excellently reviewed by Gutierrez (79), Foley (80), and others (89-97). The first case of dystocia due to ectopic pelvic kidney was described by Hohl (1) in 1828. A pelvic mass described at delivery of two normal term babies was revealed at autopsy, performed years later, to be a pelvic kidney. The first case described in the English literature appeared in the New York Medical Journal in 1888, reported by Munde (8). Cragin (14) reviewed 5 cases collected up to 1898 and added one of his own. Cragin's case is remarkable in that he performed vaginal nephrectomy of a hydronephrotic left kidney during the last month of pregnancy and succeeded in delivering a normal baby with a live mother as a final result. Wilson (81) in 1911 increased the number of cases to 10, with 28 labors resulting in 5 fetal and 2 maternal deaths. However, in the same year, J. H. Girard (82) published a thesis at the University of Paris entitled "L'ectopie simple congenitale du rein" in which he described 31 mothers having ectopic kidneys with 109 total pregnancies. Five cases had 13 abortions. In 13 labors intervention was obligatory: 83 labors ended in spontaneous deliveries. Half of the latter were easy labors; the other half were long and difficult, finally ending in spontaneous delivery. Girard's monograph has been overlooked by many reporters on the subject of dystocia with ectopic pelvic kidney. He had collected 21 more cases from the literature than Wilson. Closer scrutiny of Girard's cases enabled us to delete 5 of the group because they were iliac ectopic kidneys and offered no difficulty in pregnancy.

In a general survey of the world's literature on the subject of ectopic pelvic kidney anomalies associated with pregnancy, the French literature is represented by the excellent reviews of Girard (82) and Chapuis (107) and more recently in 1928 by Ramos (42). The German papers of Stephan (83), Hazelhorst (37), Guggisberg (45), and the recent paper by Szendi (64) review the problem thoroughly. In Italian, the work of Scontrino (43) is one of the best general reviews. Hohl (53) and Umbricht (66) have reported reviews and cases occurring in Switzerland.

Except for the monograph by Girard (82) published in 1911, all reviews on this subject have been incomplete. With the exception of Wilson's (81) no subsequent survey of the specific subject of dystocia due to ectopic pelvic kidney has appeared in the American and English literature. Isolated single case reports have appeared, however. In a short paragraph, Thompson and Pace (58), who reviewed 88 cases of ectopic kidney at the Mayo Clinic, noted that 21 of their patients had been pregnant. Fourteen of these mothers had one or more children without difficulty, and 5 had one or more miscarriages and no full term infants. One woman had a stillborn at term and another had her first child by difficult forceps and two subsequently by cesarean section.

In an attempt to correlate this information and improve the literature on ectopic pelvic kidney anomalies complicating labor and pregnancy, tables of all previous cases reported from the years 1828 to 1948 were prepared. These tables show the time of diagnosis and presenting complaint in relation to the pregnancy, the type of kidney anomaly, the number of deliveries, the outcome of babies and mothers and general follow-up of each case reported in the previous literature.

		9 yrs. after deliv. pelvic mass	Left	0	0	1	Spont.	1 alive	Alive	Normal delivery.
Goulioud (1896)	38	In 4th month of 7th pregnancy. Sacral pain	Right	3	0	7	Spont.	7 died	Died	Died following an intestinal operation following delivery.
Winter (1897)	—	During pregnancy. Pelvic mass	Left	0	0	1	Spont.	Alive	Alive	Not much data on details.
Crigin (1898)	25	At 8½ mos. of preg. Tumor behind cervix	Left	0	0	3	Spont.	3 alive	Alive	Vaginal nephrectomy followed by normal delivery (hydronephrosis).
Oliva (1898)	—	At autopsy. Eclampsia & convuls.	Horseshoe	0	0	1	Craniotomy	1 died	Died	Horseshoe kidney with eclampsia. Manual dilatation of cervix followed by craniotomy.
Baldwin (1899)	60	Many years after pregnancy. Pelvic pain	Left	0	0	5	Spont.	5 alive	Alive	Hydronephrosis & sarcoma of kidney developed at 60 yrs. of age.
Frank (1899)	30	After pregnancies. LLQ pain	Left	0	0	8	8 Spont.	8 alive	Alive	Associated & absence of left tube & ovary, congenital. Nephropexy was done.
Hochenegg (1900)	52	After pregnancies. Lumbar pain. Nephrectomy	Left	4	0	3	3 breech	3 alive	Alive	Prolonged & difficult breech delivery. No knowledge of pelvic kidney until 52 years of age.
Brooks (1900)	28	3rd month of 2nd pregnancy. Cramplike abdominal pains	Right	1 twins	0	1	Spont.	1 alive	Died	Died of acute hemorrhagic nephritis. Pelvic kidney thought to have been injured by enlarging uterus.
Bland Sutton (1901)	—	During delivery. Pelvic mass	Left	0	0	1	Spont.	1 alive	Alive	Normal delivery.
Dewis (1901)	—	After pregnancies. Laparotomy	Left	3	0	2	Spont.	2 alive	Alive	Discovered several months after delivery.

TABLE III
Cases in the Literature of Pelvic Ectopic Kidney Anomalies Associated with Pregnancy (1828-1948)

AUTHOR AND YEAR	AGE	TIME OF DIAGNOSIS, PRESENTING COMPLAINT	KIDNEY INVOLVED	NO. OF PREGNANCIES			METHOD OF DELIVERY	OUTCOME		REMARKS—FOLLOW-UP
				Abor- tions	Prematur- es	Full Term		Babies	Mother	
Hohl (1828)	—	At autopsy (75 yrs.). None	Left	0	0	2	Spont.	2 alive	Alive	Died at age of 75. Autopsy revealed pelvic kidney.
Mangiagalli (1876)	28	During labor (4th preg.). Dystocia (mass in pelvis)	Left	0	0	4	Spont.	4 alive	Died	Hydronephrosis of kidney. Punctured kidney followed by spontaneous delivery.
Wina (1874)	64	At autopsy	Left	1	0	2	Spont.	2 alive	Alive	Died at age of 65 of heart disease.
Huter (1880)	—	During delivery. Mass in front of head	Left	0	2	0	Spont.	2 died	Died	Died after 2nd delivery of edema of lungs.
Fischel (1885)	—	During 3rd pregnancy. Tumor over sacrum	Left	0	0	4	2 Spont. 2 Trans.	3 alive 1 died	Alive	Difficult labors even with premature induction of labor.
Freund (1885)	—	At autopsy	Left	0	1	1	Induct. Spont.	2 alive	Died	Pt. died of pulmonary edema after induction of premature labor.
Tenchini (1887)	60	At autopsy	Bilat.	2	0	0	—	—	Alive	Died of pneumonia at age of 60.
Munde (1888)	21	After delivery. Tumor mass, pelvis	Left	0	0	2	Spont.	2 alive	Alive	Laparotomy several months after delivery with nephrectomy.
Runge (1891)	—	After 5th pregnancy. Pelvic tumor	Left	0	0	8	7 Spont. 1 Vers. & ex-tract.	7 alive 1 died	Alive	Flat rachitic pelvis; induction of labor. Difficult version and extraction. Fractured arm in baby
Albers-Schonberg (1894)	—	Postpartum (5th d.). Tumor in pelvis	Left	0	0	3	2 Spont. 1 Vers. & ex-tract.	1 alive 2 died	Died	3 difficult labors, 3rd complicated by ruptured uterus. Patient died on 5th P.P. day.

Tiip (1912)	37	At autopsy P.P. Endometritis and pelvic phlebitis	Right	0	0	2 twins	Spont.	1 alive	Died	Died of puerperal infection 12 days after delivery. Bleeding in right kidney. Kidney discovered years after pregnancy at laparotomy.
Kelly & Burnam (1914)	—	Years after pregnancy. Mass in pelvis	Left	0	0	2	Spont.	2 alive	Alive	Kidney divided and attempt to move up into abdomen was successful. Not much information.
Bugbee & Losee (1910)	32	After 4th pregnancy. Mass in vagina	Fused Kidney	0	0	4	Spont.	4 alive	Alive	Kidney pushed out of pelvis. Protracted second labor completed by C. S. Normal follow-up.
	24	During 6th month of 1st pregnancy vomiting and bearing down sensation	Left	0	0	1	Spont.	—	Alive	Aborted 2 months after laparotomy. No further follow-up.
	22	After pregnancy. Dystocia	Left	0	0	1	Spont.	—	Alive	Patient sterilized because of fear of infections with future pregnancies.
Bompiani (1923)	30	During labor of 3rd pregnancy. Obstructed labor	Right	0	0	3	2 Spont. 1 C.S.	2 died 1 died	Alive	After 2 difficult labors & 2 abortions. Floating head necessitated C.S.
Williams (1923)	—	Before pregnancy. Previous laparotomy	Left	0	0	1	Spont.	Alive	Alive	No fallopian tube, ovary or round ligament in lt. adnexa.
Hazelhorst (1923)	42	During 2nd pregnancy ovarian mass or fibroid	Left	0	0	2	Spont. C. S.	Alive	Alive	
Schmetz (1923)	—	During 3rd month of 1st pregnancy. Lower abdominal pain	Left	1	0	0	Abortion	—	Alive	
Darner (1924)	19	After pregnancy. Pelvic inflammatory disease	Left	2	0	0	—	—	Alive	
Mennet (1927)	27	During 4th pregnancy. Pelvic tumor	Left	2	0	3	Breech Trans. C.S.	Died Died Died	Alive	
	34	During labor with 3rd child. Transverse presentation. Pelvic tumor.	Left	0	0	3	2 Spont. 1 C.S.	3 alive	Alive	

TABLE III—Continued

AUTHOR AND YEAR	AGE	TIME OF DIAGNOSIS, PRESENTING COMPLAINT	KIDNEY INVOLVED	NO. OF PREGNANCIES			METHOD OF DELIVERY	OUTCOME		REMARKS—FOLLOW-UP
				Abortions	Prematurities	Full Term		Babies	Mother	
Kehrer (1903)	38	Yrs. after pregnancy. Pelvic & low back pain	Left	0	0	5	Spont.	5 alive	Alive	Prolonged labors but spontaneous deliveries in all 5 pregnancies. Punctured kidney which contained pus. Developed nephrovaginal fistula.
Delkeskamp (1904)	23	During 3rd month of first pregnancy. Vomiting & pain in RLQ	Left	0	0	1	Spont.	1 died	Alive	Died 6 months postpartum following partial nephrectomy on a diseased single kidney.
Dufour (1904)	20	6 months postpartum right lower flank pain	Solitary kidney	0	0	1	Spont.	Alive	Died	Died several years after pregnancies. Nephrectomy 2 years after pregnancy. Febrile puerperium.
Balika (1905)	26	Years after pregnancy. Tumor in pelvis	Left	0	0	2	Spont.	2 alive	Alive	After 2 normal spontaneous deliveries a 3rd delivery necessitated craniotomy. No complications with pregnancies. Nephrectomy years later.
Orth (1905)	30	2 yrs. postpartum. Sacral pain	Left	0	1	0	Spont.	1 alive	Alive	Nephropexy followed by abortion.
Cohn (1906)	31	After pregnancy. Cystoscopic invest.	Left	0	0	1	Spont.	1 alive	Alive	Kidney almost filled pelvis. Removed kidney & patient delivered 6 days later.
Windrath (1907)	—	During 3rd pregnancy. Mass in pelvis	Left	0	0	3	2 Spont. 1 Craniotomy	2 alive 1 dead	Alive	
Loewit (1909)	49	Several yrs. after pregnancy. Lower abdominal pain	Left	0	0	6	Spont.	6 alive	Alive	
Halban (1910)	23	During 6th month of 1st pregnancy. Vaginal examination	Left	1	0	0	—	—	Alive	
Kontorowicz (1911)	24	During pregnancy. Hydro-nephrotic kidney	Right	0	0	1	Breech Spont.	1 alive	Alive	

Abruzzese (1930)	20	During labor. Failure of head to engage	Left	0	0	2	Spont. C. S.	Alive	Alive	Cesarean hysterectomy to prevent further birth complications.
LaFitte & Smith (1930)	25	During 2nd month of 2nd pregnancy. Suspected ectopic preg.	Right	0	0	2	C. S.	Alive	Alive	At laparotomy biopsy of tumor revealed it to be kidney.
Markus (1931)	34	After pregnancy. Laparotomy (bizarre pain)	Left	1	2	0	Spont.	Alive	Alive	Confused diagnostic problem.
Spinelli (1931)	32	During 7th month of 1st pregnancy. Vaginal bleeding (tumor)	Left	0	1	1	C. S.	Alive	Alive	Interrupted 1st pregnancy because of tumor in pelvis.
Belard (1931)	20	During last month of 2nd pregnancy. Tumor in pelvis	Left	0	0	2	1 forceps 1 C.S.	Alive	Alive	Nephrectomy in 5th month of 2nd pregnancy followed by successful vaginal delivery.
Hohl (1932)	37	During labor of 2nd pregnancy. Protracted labor	Right	0	0	2	1 Spont. 1 C. S.	Alive	Alive	Incised into mass at time of C. S. to tell that tumor was kidney.
LeLorier & Mayer (1934)	27	During 4th month of 7th pregnancy. Lumbo-iliac pain	Left	3	1	3	3 spont. 1 C. S.	Alive	Alive	First labor 5 days' duration followed by difficult forceps. Protracted labor in 2nd pregnancy with C. S. Bicornate uterus.
Riley (1935)	21	During labor. Dystocia, ovarian cyst	Solitary kidney	0	0	1	C. S.	Alive	Alive	Mother developed eclampsia. P. P. Well 3 weeks later.
Cordun (1937)	33	4th month of preg. Abdominal tumor	Left	1	0	1	C. S.	Alive	Alive	Details are lacking.
Omodeo-Zorini (1937)	26	During 7th month of 4th pregnancy. Vaginal examination	Right	0	0	4	3 breech	Alive	Alive	After 3 difficult breech deliveries pelvic kidney diagnosed & baby successfully delivered by C. S.

TABLE III—Continued

AUTHOR AND YEAR	AGE	TIME OF DIAGNOSIS, PRESENTING COMPLAINT	KIDNEY INVOLVED	NO. OF PREGNANCIES			METHOD OF DELIVERY	OUTCOME		REMARKS—FOLLOW-UP
				Abor-tions	Prema-tures	Full Term		Babies	Mother	
Idel (1927)	34	During labor. Mass in pelvis	Solitary	0	0	7	6 Spont. 1 C. S.	7 alive	Alive	Solitary pelvic kidney removed at time of C. S. Died postoperatively of hemorrhage.
Peralto-Ramos (1928)	25	During 8th month of pregnancy. Routine pelvic examination (cystoscopy)	Left	0	0	1	C. S.	Alive	Alive	Generally contracted pelvis C. D. 10. cm. Several hours' labor—no descent of head.
Scontrino (1928)	26	During labor. Mass in pelvis	Left	0	0	1	C. S.	Alive	Alive	Associated with absence of adnexa on left side.
Geintz (1928)	24	After pregnancies. Pain on intercourse	Horse-shoe	2	0	0	—	—	Alive	Both tubes resected because of fear of future pregnancy.
Guggisberg (1928)	—	After pregnancies. Mass in pelvis (cystoscopy)	Left	2	0	3	Spont.	3 alive	Alive	Normal deliveries.
—	—	After 2nd pregnancy. Mass in pelvis. Cystoscopy	Left	0	0	3	2 Spont. 1 C. S.	3 alive	Alive	After 2 normal deliveries. Worry about damage to kidney decided C. S.
—	—	After 2nd pregnancy. Mass in pelvis	Left	0	0	3	1 breech 1 trans. 1 C. S.	2 died	Alive	2 difficult deliveries followed by C. S.
McCown (1920)	20	3 months after abortion. Mass in pelvis. Pain	Bilat.	1	0	0	—	—	Alive	Bilateral renal ectopia. No full term delivery.
Pease (1920)	—	During 2nd pregnancy. Tumor in pelvis	Left	0	0	2	Spont. C. S.	Alive	Alive	Normal delivery followed by cesarean section.
—	—	During 2nd pregnancy. Tumor in pelvis	Left	0	0	2	Spont. C. S.	Alive	Alive	14 hr. labor with 1st child. Both cases elective C. S. done without trial labor.

Nachman (1944)	—	After pregnancy. Devel- oped urinary symptoms	Left	0	0	3	Spont.	2 alive	Alive	Developed tuberculous of ectopic pelvic kidney years later. Floating head in primiparous labor. Right pelvic kidney ascer- tained with left pelvic kid- ney & spleen bilobed. Baby thought to have died of anoxia. Confused in ovarian tumor. C. S. done with fully dilated cervix. Pyelitis developed just be- fore delivery. Feared vagi- nal delivery in C. S. was done.
Umbrecht (1944)	23	During labor 1st pregnancy. Rectal examination	Right	0	0	1	C. S.	Alive	Alive	
	22	Before pregnancy. Stress incontinence	Right	0	0	1	C. S.	Dead	Alive	
Siegel (1946)	20	Pelvic exam. at delivery. Cervix fully dilated (ovarian tumor)	Left	0	0	1	Brooch C. S.	Alive	Alive	
Presno Bas- tiony (1946)	37	Before pregnancy. Pain	Fused kidney	1	0	1	Trans. C. S.	Alive	Alive	
Colo & De- lanoy (1946)	—	During 2nd pregnancy. Transverse presentation	Left	0	0	2	Trans. 2 C. S.	2 alive	Alive	
Sala-Ponsati (1947)	38	After pregnancy. Pelvic mass	Left	0	0	3	3 spont.	3 alive	Alive	Normal easy delivery.

REVIEW

TABLE III--Continued

AUTHOR AND YEAR	AGE	TIME OF DIAGNOSIS, PRESENTING COMPLAINT	KIDNEY INVOLVED	NO. OF PREGNANCIES			METHOD OF DELIVERY	OUTCOME		REMARKS--FOLLOW-UP
				Abortions	Prematures	Full Term		Babies	Mother	
Omodeo-Zorini (1937)	30	4 yrs. after pregnancy. No symptoms	Bilat.	0	0	1	C. S.	1 alive	Alive	Bilateral pelvic kidneys. Diagnosed 4 yrs. after C. S.
		In a general study of a large series of 97 cases, 21 women had been pregnant. Not much obstetrical data available		5	0	16	14 Spont. 1 forceps. 1 C. S.	1 died 15 alive	Alive	Only 1 dead child in 16 babies of which 15 delivered vaginally. Normal deliveries.
Davidson (1938)	33	Diagnosed years after deliveries. Mass in pelvis	Left	0	0	3	Spont.	3 alive	Alive	Solitary pelvic kidney. Hysterectomy done to prevent future pregnancies. Rachitic and severely contracted pelvis. Bilateral ectopic pelvic horse-shoe kidney. Developed pyelitis in puerperium. Died 6 yrs. after last pregnancy. Kidney failure. Only 40 Gms. kidney tissue found at autopsy. Developed hydronephrosis during pregnancy. Refused nephrectomy. Was well, several months follow-up.
		During 7th month of pregnancy. Back pain	Solitary	0	1	0	Cesarean Hysterec.	1 died	Alive	
Siegmund (1940)	32	At term. Mass in pelvis	Left	0	0	1	C. S.	Alive	Alive	
Fitzgerald (1940)	19	During 9th month of pregnancy. "Fibroid"	Horse-shoe	0	0	1	C. S.	Alive	Alive	
Ockerblad & Carlson (1940)	36	After pregnancy. Chronic albuminuria	Solitary	0	0	2	Spont.	2 alive	Alive	
Szendli (1942)	30	2nd month of 6th pregnancy. Ovarian tumor (goose egg)	Left	0	0	6	1 trans. 4 spont. 1 C. S.	4 alive 2 died	Alive	

Although the outlook for the mother with pelvic ectopic kidney anomalies has improved considerably (no deaths in 48 cases reported since 1928), the fetal mortality remains between 14 and 16 per cent. The incidence of abortion (15.4%) and prematurity (3.9%) is not apparently increased over the normal frequency for these factors.

As pointed out in the discussion of embryology, many bizarre kidney anomalies may occur. In the 98 cases associated with pregnancy described in the literature several different types of ectopia have occurred. These cases have been cataloged under a slight modification of the classification used by Bell (76), Everett (77) and Gutierrez (79) (Table V). Most of the cases (85) have been of the simple unilateral pelvic ectopia type. In 64 cases in which the exact kidney (right or

TABLE V

Classification of Various Types of Pelvic Ectopic Kidney Anomalies Associated with Pregnancy in the Previous Literature—Years (1828-1948)

TYPE OF KIDNEY ANOMALY	NUMBER OF CASES
I. Simple unilateral pelvic ectopia.....	85
(a) Right kidney.....	9 (14%)
(b) Left kidney.....	55 (86%)
Unknown.....	21
Note: Five cases associated with hydronephrosis	
II. Bilateral pelvic ectopia without fusion.....	3
III. Bilateral pelvic ectopia with fusion.....	5
(a) Horseshoe kidney.....	3
(b) Fused kidney.....	2
IV. Solitary pelvic kidney.....	5
V. Crossed pelvic kidney.....	0
Total.....	98

left) was known, 86% were left kidneys and 14% were right kidneys. This study compares with other studies on renal ectopia in the general population as follows:

Author	Left kidney	Right kidney
Karschulin (89).....	47 (71%)	19 (29%)
Bell (76).....	18 (51.4%)	17 (48.6%)
Thompson and Pace (58).....	40 (46%)	46 (54%)
Pregnant cases.....	55 (86%)	9 (14%)

The remaining 13 cases were of even greater interest since in 8 of these instances both of the kidneys were in the pelvis (3 were unfused and 5 cases were examples of horseshoe kidney or fused kidney) and the remaining 5 cases were solitary kidneys. Figure 1 presents graphic portrayal of the classification of various types of pelvic ectopic kidney anomalies associated with pregnancy observed during the years 1828-1948.

TABLE IV
Summary of the Literature of Deaths occurring in Cases of Pregnancy Associated with Pelvic Kidney Anomalies (1828-1948)

AUTHOR & YEAR	AGE	PARITY	CLINICAL COURSE, CAUSE OF DEATH	TYPE OF KIDNEY ANOMALY	METHOD OF DELIVERY	OUTCOME OF BABY	TIME OF DEATH
Mangiagalli (1876)	28	4	During labor large pelvic mass was punctured. Proved to be hydronephrosis. Died of multiple infection	Left ectopic pelvic kidney	Spontaneous	Alive	Immediate puerperium
Huter (1880)	—	2	Died after delivery of pulmonary edema	Left ectopic pelvic kidney	Spontaneous	Dead	Immediate puerperium
Freund (1885)	—	2	Died of pulmonary edema after induction of premature labor	Left ectopic pelvic kidney	Spontaneous after medical induction	Alive	Immediate puerperium
Albers-Schönberg (1894)	—	3	After difficult labor. Version and extraction was done. Died of ruptured uterus	Left ectopic pelvic kidney	Version and extraction	Dead	5th day postpartum
Rosthorn (1896)	38	10	Developed intestinal obstruction after delivery and died after laparotomy	Right ectopic pelvic kidney	Spontaneous	Dead	Immediate puerperium
Oliva (1898)	—	1	Developed eclampsia. Manual dilatation of cervix and craniotomy followed by death	Pelvic horseshoe kidney	Manual dilatation of cervix	Dead	During delivery
Brooks (1900)	28	2	Died in 3rd month of 2nd pregnancy of acute hemorrhagic nephritis	Right ectopic pelvic kidney	Aborted	Dead	During 3rd month of pregnancy
Dufour (1904)	20	1	Died 6 months postpartum of complications during birth. On solitary pelvic kidney, partial nephrectomy attempted	Solitary pelvic kidney	Spontaneous	Alive	6 months postpartum
Tilp (1912)	37	2	Died of puerperal infection following delivery of twins	Right ectopic pelvic kidney	Spontaneous	Alive	12th day postpartum
Idel (1927)	34	7	Solitary kidney removed at time of cesarean section. Died of hemorrhage postoperatively	Solitary kidney	Cesarean section	Alive	Postoperatively

bility casually but no specific references were quoted. In his review of crossed ectopia, Wilmer found 236 cases of unilateral fused kidney. He noted two cases in which the position and size of the renal mass offered an obstruction that necessitated cesarean section, but since exact details were not given these cases were not added to our review.

Fitzgerald (62), in 1940, after a very exhaustive search of the literature, concluded that his case of pelvic horseshoe kidney in a 19 year old primipara was the only recorded case of this particular type of pelvic ectopic kidney anomaly associated with pregnancy. This statement is not entirely accurate, since Bugbee and Losee (34) divided a pelvic horseshoe kidney in 1919 after the patient had 4 spontaneous labors. Geinitz (44), in 1928, and Oliva (15) as early as 1898, described pelvic horseshoe kidney associated with pregnancy. Oliva's (15) case is particularly interesting. The patient entered the hospital with eclampsia, having convulsions. Her cervix was manually dilated and craniotomy performed on the infant. Both mother and baby died shortly thereafter. The horseshoe kidney was discovered lying in the true pelvis at autopsy.

Solitary pelvic kidneys have been described five times associated with pregnancy. Two of the cases had eclampsia. In the third case, that of Fuchs (60), in 1938, cesarean hysterectomy was done to prevent future pregnancies. The fourth case of solitary kidney was observed by Ocherblad and Carlson (63) 6 years after 2 spontaneous labors with live full term infants. At death, only 40 grams of kidney tissue remained. In a fifth case, that of Dufour (24), the patient died 6 months postpartum following partial nephrectomy in an attempt to preserve the remaining kidney cortex from infection.

Analysis of the method of delivery in relationship to the type of pelvic ectopic kidney anomaly is illustrated in Table VI. This table tends to show that the method of delivery, with the exception of breech and version and extraction, causes very little change in the fetal mortality rate. Of 182 full term infants, 133 delivered spontaneously with the loss of 13 (9.8%). Of 31 infants delivered by cesarean section, 3 were lost (9.6%). Version and extraction and breech delivery occurred only a few times. The fetal mortality rates were 80% and 50% respectively. In 182 full term pregnancies, 8 transverse presentations occurred (4.3%).

Among the many complications of pregnancy or the kidney observed in 98 mothers the following may be listed.

Very difficult labors.....	14 cases
Nephrectomy during pregnancy.....	5 cases
Hydronephrosis during pregnancy.....	5 cases
Premature induction of labor.....	5 cases
Postpartum pyelitis.....	5 cases
Markedly contracted pelvis.....	4 cases
Sterilization for fear of future pregnancy and injury to the kidney.....	4 cases
Adnexal anomalies—absence of tube or ovary on one side.....	3 cases
Floating head at time of labor.....	3 cases
Puncture of hydronephrosis at time of delivery.....	3 cases
Eclampsia.....	2 cases

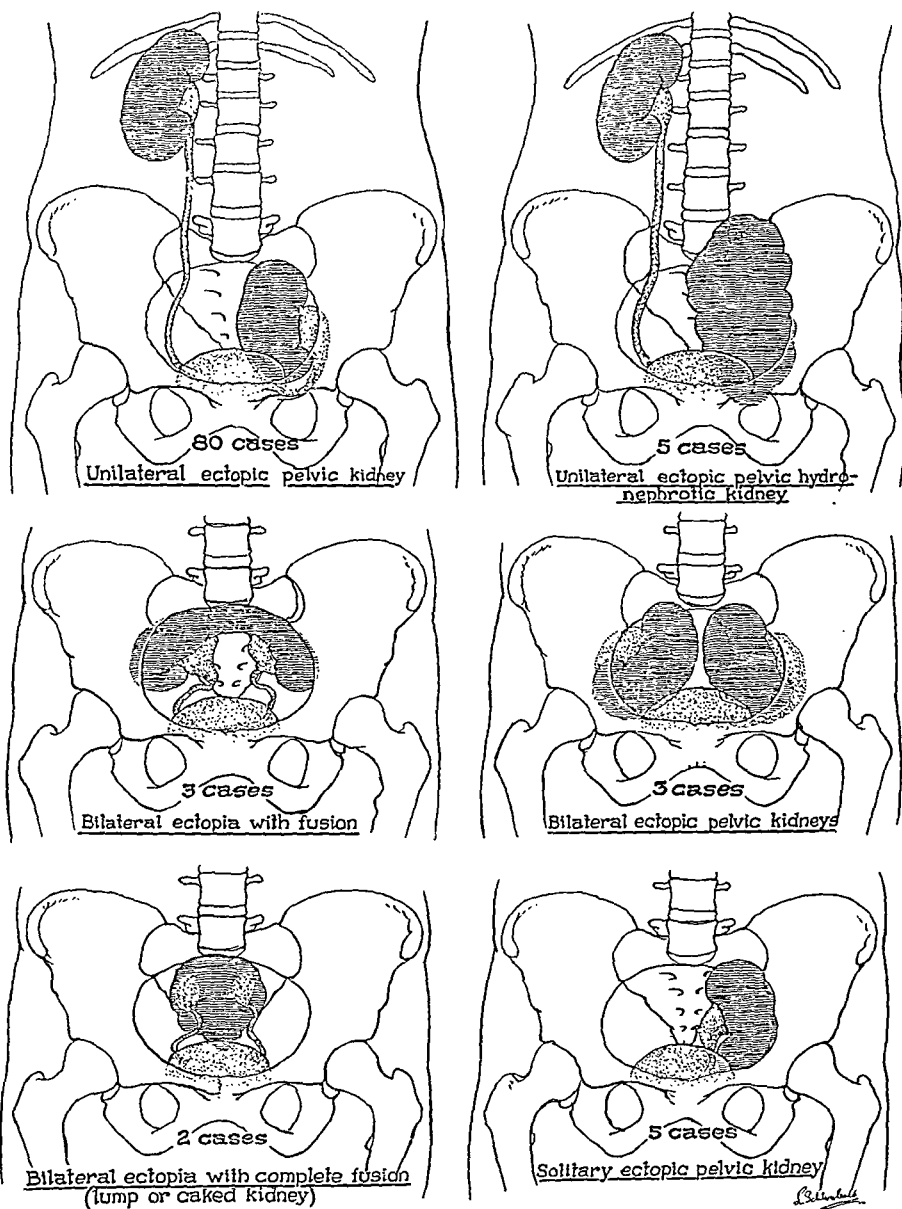


FIG. 1. Graphic portrayal of the various types and number of pelvic ectopic kidney anomalies associated with pregnancy observed by various authors in the world's literature between the years 1828 to 1948.

Crossed pelvic ectopia, with or without fusion, associated with pregnancy, has not been recorded in the literature to the best of our knowledge. However, in a paper on crossed renal ectopia with fusion, Wilmer (90) mentioned this possi-

TABLE VII
Cases of *Dystocia due to Movable Kidney* Reported in the Literature (1904-1948)

AUTHOR & YEAR	AGE	TIME OF DIAGNOSIS, PRESENTING COMPLAINT	KIDNEY INVOLVED	NO. OF PREGNANCIES			METHOD OF DELIVERY	OUTCOME		REMARKS & FOLLOW-UP
				Abor-tions	Prema-tures	Full term		Baby	Mother	
Gratschoff (1904)	29	During labor. 2nd pregnancy. Small tumor in pelvis	Right	0	0	2	Spontan. Craniot.	1 alive 1 dead	Alive	Kidney prolapsed before delivery. Returned to abdomen 2 weeks P.P.
Ely (1909)	—	During labor. Ruptured uterus. Hysterectomy	Right	0	0	1	Spontan.	Dead	Dead	P.P.II. Kidney prolapsed into rupture site. Patient died of sepsis.
Bissell (1910)	41	After 1st delivery. Tumor in pelvis. Laparotomy	Right	0	1	2	Bag. dil. Vers. & Ext.	1 alive 1 alive	Alive	3rd preg. Premature induction of labor resulted in small baby.
Wilson (1911)	21	During 2nd stage. Tumor in pelvis	Right	0	0	1	Vers. & Ext.	1 dead	Alive	After several hours of labor kidney forced back into abdomen.
Vogt (1931)	—	During labor 1st preg. Threatened uterine rupture. C.S.	Right	0	0	2	Spontan.	2 alive	Alive	2 yrs. after 1st labor 3 signs of threatened rupt. of uterus pt. delivered vaginally.
Burger (1938)	24	9th mo. of preg. pelvis & abdom. tumor.	Right	0	0	1	Cesarean Spontan.	Alive	Alive	Nephrectomy was done after delivery.
Szendl (1942)	34	Nephrectomy During 3rd pregnancy. Fist sized tumor in pelvis	Left	0	0	3	Spontan.	3 alive	Alive	Hydronephrosis in movable kidney; 7 yrs. later kidney size of 9 mos. pregnancy.
Umbricht (1944)	—	During 2nd preg. Curettage for abor. Cystoscopy	Left	1	0	1	Spontan.	Alive	Alive	During curettage punctured orange sized tumor in pelvis. Bladder filled with blood.

Biopsy of pelvic mass to establish diagnosis of kidney.....	2 cases
Bleeding into pelvic kidney.....	2 cases
Spina bifida associated with pelvic ectopic kidney.....	1 case
Acute hemorrhagic nephritis.....	1 case

Because of the confusion in the literature on the differential diagnosis of dystocia due to true congenital pelvic ectopic kidney anomalies and the entity of movable or "floating" kidney it was deemed advisable to include the few cases reported in a separate Table VII. Eight cases have been reported, of which 6 have been right kidneys and 2 left kidneys. These 8 mothers had a total of 15 pregnancies with one abortion, one premature and 13 full term infants. Of the 13 full term infants, 3 died and 10 lived. Five operative deliveries were

TABLE VI

*Comparison of the Fetal Mortality to Method of Delivery in Mothers with Pelvic Renal Ectopia
(182 Full Term Deliveries from 1828-1948)*

TYPE OF RENAL ANOMALY	SPONTANEOUS		FORCEPS		BREECH		VERSION & EXTRACTION		CESAREAN		TOTAL	
	Number of cases	Fetal deaths	Number of cases	Fetal deaths	Number of cases	Fetal deaths	Number of cases	Fetal deaths	Number of cases	Fetal deaths	Number of cases	Fetal deaths
Unilateral pelvic ectopia....	120	13 (10.8)	1	1	10	5 (50.0)	5	4 (80.0)	26	3 (11.5)	162	26 (14.8)
Bilateral ectopia (without fusion).....	0	0	0	0	0	0	0	0	1	0	1	0
Bilateral ectopia (with fusion).. <td>4</td> <td>0</td> <td>0</td> <td>0</td> <td>0</td> <td>0</td> <td>0</td> <td>0</td> <td>2</td> <td>0</td> <td>6</td> <td>0</td>	4	0	0	0	0	0	0	0	2	0	6	0
Solitary kidney	9	0	0	0	0	0	0	0	2	0	11	0
Total.....	133	13 (9.8)	1	1	10	5 (50.0)	5	4 (80.0)	31	3 (9.6)	180	26

Note: Three of 5 were transverse presentations delivered by version and extraction.
Five transverse presentations were delivered by cesarean section.
Two craniotomies were also performed.

performed including one craniotomy, 2 versions and extractions, one bag dilatation and one cesarean section. One mother died of a ruptured uterus followed by sepsis.

PRESENT STUDY

With the knowledge that only a few cases of ectopic pelvic kidney anomaly have been observed by any one obstetrician, it appeared beneficial to report our experiences with 14 additional cases. Seven cases of pregnancy complicated by pelvic ectopic kidney anomalies have occurred on the Obstetrical Service of The Johns Hopkins Hospital during the period 1927-1948. In this same period, 34,206 women were delivered with an incidence of pelvic ectopic kidneys to deliveries

Cases of Pelvic Ectopic Kidney Anomalies and Pregnancy Delivered at the Johns Hopkins Hospital, 1927-1948

TABLE VIII

CASE NUMBER (YEAR)	AGE	TIME OF DIAGNOSIS, PRESENTING COMPLAINT	KIDNEY INVOLVED	NO. OF PREGNANCIES			METHOD OF DELIVERY	OUTCOME		REMARKS-FOLLOW-UP
				Abortions	Prenatalures	Full Term		Baby	Mother	
U-15510 (1927)	35 (w)	After 4th pregnancy. Dx of ectopic preg. Exploration revealed pelvic kidney	Left	1	0	5	4 spont. 1 breech	Alive 5	Alive	2 children died later of "flu." 2 children after Dx of pelvic kidney delivered spontaneously.
103020 (1940)	30 (c)	Before pregnancy. Hypertensive toxemia. Pain: laparotomy	Right	1 Therapeutic	0	2	Spont. Spont.	Alive	Alive	Pelvic kidney removed because of hypertension: pathology report normal. 3rd pregnancy interrupted by hysterectomy because of only one remaining kidney. Lived 4 yrs. Died of hypertensive encephalopathy.
238404 (1942)	19 (c)	During 2nd pregnancy. Possible ectopic preg. I.V. pyelography	Horseshoe	0	0	2	Forceps Rotation C.S.	Alive	Alive	Difficult forceps, 1st Del. Because of bil. pelvic kidney C.S. was elected.
321078 (1944)	32 (c)	During 2nd pregnancy. "Ovarian tumor." Laparotomy	Left	1	0	1	Spont.	Alive Alive 1	Alive	Laparotomy during pregnancy at 16 wks. followed 8 wks. later by 680 gm. abortion.
342626 (1945)	30 (c)	After pregnancy. Uterine myomata. Hysterectomy	Right	0	0	1	Spont.	Alive	Alive	Kidney located over pelvic brim. Might be described as iliac or pelvic ectopic kidney.
408583 (1947)	23 (w)	Before pregnancies. Pelvic mass (ovarian tumor). Laparotomy	Right	2	0	0	—	—	Alive	At operation absence of appendix also noted.
414167 (1949)	18 (c)	Between pregnancies. Pelvic mass-ectopic pregnancy. Culdoscopy & laparotomy	Left	0	0	2	Forceps Spont.	Alive Alive	Alive	Extensive condyloma acuminata during 1st pregnancy limiting pelvic exams. Successfully delivered 2 full term infants vaginally.

of 1:4,886. This compares favorably with the reported incidence of pelvic ectopic kidneys in the general population (Table I). One of the cases (No. 238464) is a pelvic horseshoe kidney which is exceedingly rare and no comparable incidence rates have been published, but in our series it would be 1:34,206. Table II represents the incidence of horseshoe kidney, pelvic and abdominal, in the general population and is, therefore, not comparable. The pertinent data on these 7 cases are shown in Table VIII. In addition to these, 7 cases of ectopic pelvic kidney observed by the urologic section of the Gynecologic Service of this hospital were also included in the study and data are recorded in Table IX.

The maternal and fetal mortality of these 14 cases of pelvic ectopic kidney anomalies may be summarized as follows:

Number of mothers.....	14
Number of maternal deaths.....	0
Total number of pregnancies in 14 mothers.....	40
Total number of abortions.....	12 (30%)
Number of premature infants.....	1
Deaths of premature infants.....	1 (100%)
Number of full term infants.....	27
Deaths of full term infants.....	2 (7.4%)
Deaths of viable infants.....	3 (10.3%)
Total fetal loss in 40 pregnancies.....	15 (37.5%)

Analysis of this summary illustrates that maternal mortality is negligible during the period of pregnancy and the puerperium. One of the patients died 4 years after her last pregnancy of hypertensive disease. Her third pregnancy was terminated by hysterectomy because of the associated hypertensive toxemia. One other patient had 2 pregnancies interrupted for hypertensive toxemia; one by therapeutic abortion, and the second by cesarean section in which a premature infant (the only premature in the series) succumbed. The incidence of abortion (30%) would be only 25% if these 2 cases were deleted. The fetal mortality of 7.4% for full term infants can also be reduced since, as Table VIII illustrates, of 13 full term infants delivered in the Johns Hopkins Hospital all survived. The 2 deaths of full term infants occurred in another hospital following difficult forceps deliveries.

The method of delivery of the 27 full term infants and the outcome of the babies may be summarized as follows:

Method of delivery	Cases	Deaths (per cent)
Spontaneous.....	20	0 (0%)
Forceps.....	5	2 (40%)
Breech.....	1	0
Cesarean section.....	1	0

The above data are significant since all of the cases except one were delivered vaginally. This exception was the only example of pelvic horseshoe kidney in the 14 cases studied. This case will be described in detail but it is interesting that she had been able to deliver a previous child with what was described as a difficult forceps procedure.

TABLE VIII

Cases of Pelvic Ectopic Kidney Anomalies and Pregnancy Delivered at the Johns Hopkins Hospital, 1927-1948

CASE NUMBER (YEAR)	AGE	TIME OF DIAGNOSIS, PRESENTING COMPLAINT	KIDNEY INVOLVED	NO. OF PREGNANCIES			METHOD OF DELIVERY	OUTCOME		REMARKS—FOLLOW-UP
				Abortions	Prematurities	Full Term		Baby	Mother	
U-15510 (1927)	35 (w)	After 4th pregnancy. Dx of ectopic preg. Exploration revealed pelvic kidney	Left	1	0	5	4 spont. 1 breech	Alive 5	Alive	2 children died later of "flu." 2 children after Dx of pelvic kidney delivered spontaneously.
103020 (1940)	30 (c)	Before pregnancy. Hypertensive toxemia. Pain: laparotomy	Right	1 Therapeutic	0	2	Spont. Spont.	Alive	Alive	Pelvic kidney removed because of hypertension: pathology report normal. 3rd pregnancy interrupted by hysterectomy because of only one remaining kidney. Lived 4 yrs. Died of hypertensive encephalopathy.
238464 (1942)	19 (c)	During 2nd pregnancy. Possible ectopic preg. I.V. pyelography	Horseshoe	0	0	2	Forceps Rotation C.S.	Alive	Alive	Difficult forceps, 1st Del. Because of bil. pelvic kidney C.S. was elected.
321078 (1944)	32 (c)	During 2nd pregnancy. "Ovarian tumor," Laparotomy	Left	1	0	1	Spont.	Alive 1	Alive	Laparotomy during pregnancy at 16 wks. followed 8 wks. later by 680 gm. abortion.
342626 (1945)	36 (c)	After pregnancy. Uterine myomata. Hysterectomy	Right	0	0	1	Spont.	Alive	Alive	Kidney located over pelvic brim. Might be described as iliac or pelvic ectopic kidney.
408683 (1947)	23 (w)	Before pregnancies. Pelvic mass (ovarian tumor). Laparotomy	Right	2	0	0	—	—	Alive	At operation absence of appendix also noted.
414167 (1949)	18 (c)	Between pregnancies. Pelvic mass—ectopic pregnancy. Culdoscopy & laparotomy	Left	0	0	2	Forceps Spont.	Alive	Alive	Extensive condyloma acuminata during 1st pregnancy limiting pelvic exams. Successfully delivered 2 full term infants vaginally.

TABLE IX

Cases of Pelvic Ectopic Kidney Anomalies Associated with Pregnancy but Delivered Elsewhere—Johns Hopkins Hospital (1928-1949)

CASE NUMBER (YEAR)	AGE	TIME OF DIAGNOSIS, PRESENTING COMPLAINT	KIDNEY INVOLVED	NO. OF PREGNANCIES			METHOD OF DELIVERY	OUTCOME		REMARKS—FOLLOW-UP
				Abortions	Prematurities	Full Term		Baby	Mother	
U-16274 (1928)	35 (w)	After pregnancies. Tuboovarian mass. Pain: laparotomy	Left	3	0	2	Forceps	Died 20th d.	Alive	Difficult forceps.
U-47727 (1933)	65 (w)	After pregnancies. Pelvic mass. Exploratory laparot.	Right	1	0	7	Forceps All spontaneous	Stillb. 4 alive 3 died of dis.	Alive	No difficulty with deliveries. Some persistent urinary symptoms.
210191 (1940)	22 (w)	After pregnancy. Pain in LLQ. Nephrectomy. Cystoscopy	Left	0	0	1	Spont.	Alive	Alive	Ectopic kidney & hydronephrosis. Nephrectomy 3 years after pregnancy.
227919 (1941)	33 (w)	During pregnancy. Hypertensive disease. Kidney study	Right	1 Therapeutic	1	0	Cesarean section	Died	Alive	Both pregnancies terminated because of hypertensive disease.
413542 (1947)	65 (w)	After pregnancies. Urinary symptoms. Left nephrectomy	Bilat.	1	0	2	Spont.	Alive	Alive	Hydronephrosis developed in left kidney at 65 yrs. of age. Left nephrectomy.
491704 (1949)	47 (w)	Long after pregnancies. Medical work-up. Cystoscopy	Right	1	0	1	Spont.	Alive	Alive	During attack of pneumonia & urinary infection approximately 20 yrs. after preg.
502653 (1948)	34 (w)	After pregnancy	Right	0	0	1	Forceps	Alive	Alive	Developed hydronephrosis.

In order to give the reader a more practical approach to the problem of pelvic renal ectopia associated with pregnancy 3 cases will be presented. The first case will illustrate the management of unilateral pelvic ectopia of the kidney during labor. The second case is an excellent example of the management of pelvic horseshoe kidney and the third case demonstrates unilateral pelvic renal ectopia in a pregnancy also complicated by hypertensive disease.

ILLUSTRATIVE CASES

Case 1. Unilateral Pelvic Ectopic Kidney and Management During Labor

The patient (Mrs. L. H. #414167) a colored married woman, 18 years of age was first seen in the Obstetrical Dispensary on February 25, 1947. At this time, she was found to be 23 weeks pregnant, complicated by extensive condylomata acuminata which filled the vaginal canal as a fungating, discharging, foul smelling mass. The patient was hospitalized on two occasions before delivery for penicillin and blood transfusion therapy in an attempt to control the vaginal infection. The patient resisted vaginal examinations and finally entered the hospital in labor and delivered a 3040 gram male infant without difficulty. No knowledge of the kidney anomaly was divulged in this first pregnancy.

One year later, March 15, 1948, the patient was examined in the Obstetrical Dispensary because of 4 months amenorrhea. No pregnancy was present at this time but a 5 x 5 x 6 cm. mass was described in the left adnexal region. A presumptive diagnosis of ectopic pregnancy was made. On April 3, 1948, the patient was culdoscoped. The uterus, ovaries and tubes were not remarkable but a whitish mass covered by dilated blood vessels was observed in the cul de sac region. Laparotomy was performed revealing the mass to be a unilateral left pelvic ectopic kidney. The patient had an uneventful recovery and was subjected to intravenous pyelography which revealed normal kidney outlines on the right and the calices of the left kidney at the level of the first sacral vertebra (fig. 2A). On a subsequent visit to the Cystoscopy Clinic, retrograde pyelography was attempted on the left side but it was impossible to insert the catheter into the ureteral orifice on that side. Indigo carmine injected intravenously, however, appeared in the left ureteral orifice in 5 minutes, indicating good function in the left pelvic kidney.

The patient became pregnant shortly thereafter and registered for prenatal care on October 28, 1948. Her expected date of confinement was March 11, 1949. Her prenatal course was uneventful until March 10, 1949. On that date, the patient was admitted to the hospital because of slightly elevated blood pressure. Rectal examination revealed that the pelvic kidney could be felt distal to the head and extending down to the level of the ischial spines. On March 11, 1949, labor started. Sterile vaginal examination revealed the head of the baby to be only dipping into the true pelvis. X-ray pelvimetry was obtained which revealed an adequate pelvic capacity. Prodromal labor followed for 24 hours, but by noon of March 12, 1949, labor pains were of good quality. By 5 P.M., the vertex had descended to the level of the ischial spines and the cervix was 3 cm. dilated. Catheterized urine examinations failed to show evidence of bleeding in the urinary tract. At this time the kidney was definitely movable and was not being compressed or wedged between the vertex and the sacrum. At 6:30 P.M., the patient was taken to X-ray for an intravenous pyelogram which showed that the left kidney was functioning since the kidney pelvis was clearly outlined (fig. 2B). The patient returned to the delivery floor at 7:30 P.M. and at 7:50 P.M. her membranes spontaneously ruptured with the cervix 8 cm. dilated and the head on the perineal floor. Spontaneous delivery of a 3375 gram female infant took place at 8 P.M., March 12, 1949. A small cervical laceration on the right side of the cervix was repaired. The left kidney was found to be located at the pelvic brim at completion of delivery. Catheterized urine drawn after delivery contained only 7 red blood cells per high power microscopic field. The patient's postpartum course was uneventful. The patient returned to Cystoscopy six weeks later and urologic investigation was completely normal.

This case illustrates the mechanism by which a unilateral pelvic ectopic kidney can be bypassed by the vertex of the oncoming fetal head. This is illustrated in figure 3. The mechanism is similar to the action of labor in patients with fibromyomata located in the lower portion of the uterus, particularly as observed with cervical fibroids. Numerous vaginal examinations done during the course of the labor and the intravenous pyelogram taken just before delivery support the mechanics of the diagram illustrated in figure 3.



FIG. 2 (A). Case number 1. Mrs. L. H. Illustrates intravenous pyelogram, taken between pregnancies. Right kidney is in normal position while left kidney is in the true pelvis.

(B). Intravenous pyelogram taken 45 minutes before delivery of case illustrated in (A). Kidney has ascended out of pelvis. At this point kidney is still functioning and illustrates how kidney and fetal head accommodate to pelvic capacity. (Films have been retouched to aid visualization for the reader.)

Case 2. Bilateral Pelvic Ectopic Kidney with Fusion (Pelvic Horseshoe Kidney)

The patient (Mrs. V. G. #238464) a 19 year old colored married woman was first seen in the Obstetrical Dispensary on September 16, 1941. At this time, she was 28 weeks pregnant. No other findings were present at this time and the patient was registered as a normal primigravida. During her prenatal care, x-ray pelvimetry was obtained because of a breech presentation. The pelvic measurements revealed an adequate pelvic capacity. Her prenatal course was otherwise uneventful and on December 13, 1941 she was admitted to the delivery floor in active labor. Because of a "floating head" a sterile vaginal examination was done after 3 hours of labor. The cervix was 4 cm. dilated and a vertex with occiput posterior was presenting at a level of 2 cm. above the spines. The examiner felt a "rectosigmoid mass" which was not expected to cause serious dystocia. After 14 hours of hard labor the patient was delivered of an infant weighing 3690 grams, using Kielland forceps for rotation from occiput posterior to anterior position. This procedure was de-

scribed as "quite difficult." The patient and her infant did well and were discharged in good condition.

On March 30, about 4 months after the delivery of the first infant, the patient was observed and followed by the Gynecological Service as a possible ectopic pregnancy, and finally on June 30, 1942, she was admitted to the hospital. Examination revealed a definite intrauterine pregnancy and also bilateral pelvic masses which were firm and nodular. At the suggestion of the senior gynecologist, intravenous pyelography was performed which established the diagnosis of pelvic horseshoe kidney (fig. 4B). After the urological work-up, the patient was registered in the Obstetrical Clinic and allowed to continue with her pregnancy. Considerable discussion as to the mode of delivery was entertained, but the previous difficult forceps and the possibility of injury to the kidney parenchyma decided in favor of cesarean section. Other x-rays were taken during pregnancy and resembled figure 4C.

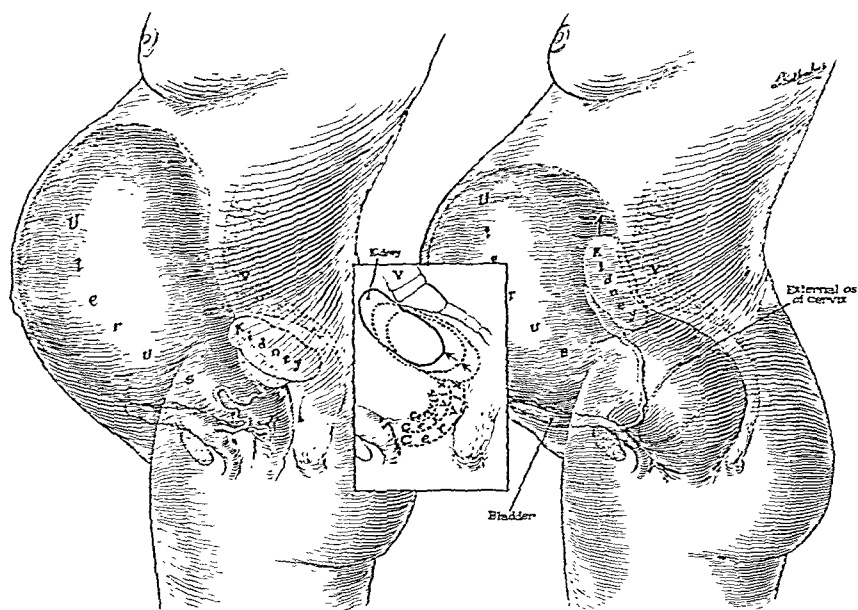
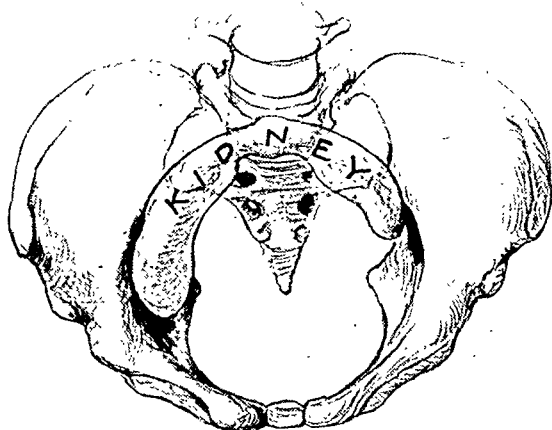


FIG. 3. Illustrates the location of the kidney at the onset of labor in unilateral renal ectopia as shown on the left and the subsequent ascent of the kidney as the fetal head descends deeper into the pelvis during the second stage of labor. The kidney also utilizes the space laterally in both inlet and midplanes of the bony pelvis.

A low cervical cesarean section was performed and a 3460 gram infant delivered without difficulty. On inspection of the pelvis following closure of the uterus, it was found that the horseshoe kidney extended about one-half to one inch above the sacral promontory and bulk of the kidneys extended over the sacrum and posterior pelvis for about 4 inches. Figure 4A is an artist's drawing made at the time of the cesarean section. The patient was also subjected to tubal resection at this time. The postoperative and postpartum course of the patient was uneventful. At the 6 weeks examination both urinary tract and genital tract were not remarkable.

This case illustrates how difficult it is to make a diagnosis of pelvic kidney unless this possibility is kept in the obstetrician's mind and also illustrates that most pelvic kidneys will permit vaginal delivery. But it should also be pointed



PELVIC HORSESHOE KIDNEY WITH PREGNANCY

A



B



C

FIG. 4 (A). Artist's conception of the shape and location of bilateral fused ectopic pelvic kidneys described in Case 2 of the text, at the time of cesarean section.

(B). Intravenous pyelogram of a case of pelvic horseshoe kidney (case 2) taken during the third month of pregnancy.

(C). Intravenous pyelogram of the same patient during the ninth month of pregnancy showing a vertex presentation of the fetus. Compare the ureters in Figures B and C which show very little increased dilatation of ureters usually associated with increase in the age of the pregnancy.

out that, with cases in which all of the kidney tissue is in the pelvis, it is probably wiser in this era of chemotherapy and safer cesarean section, to consider abdominal delivery for this particular type of pelvic kidney.

Case 3. Pelvic Ectopic Kidney associated with Pregnancy and further complicated by Hypertensive Disease

The patient (Mrs. M. H. #103020) was a 30 year old colored married woman, who in 1934 had the diagnosis established of ptosis of the right kidney. At that time, the kidney was at the level of the fifth lumbar vertebra with one pole extending into the true bony pelvis. For the next 3 years, the patient was followed closely by the Urologic Clinic. In 1937, she delivered a 3720 gram infant spontaneously, and in 1938 delivered a 3160 gram infant spontaneously without difficulty. Both babies did well. Both pregnancies were accompanied by severe toxemias and constriction of blood vessels of the retinae. In 1940 the patient was admitted to the Medical Service for investigation of her hypertension. The abnormal vascular pattern of the ectopic kidney was considered as the possible agent producing hypertension so unilateral nephrectomy was proposed. At laparotomy, the kidney extended from the brim of the pelvis down to the infundibulo-pelvic ligament on the right side. The main vessels were isolated and were found to be branched but no definite obstruction was described. The kidney was removed without difficulty and the patient withstood the procedure well. The pathological diagnosis was "kidney showing congestion and cloudy swelling." In 1942, the patient again became pregnant and at 18 weeks of the pregnancy, reasoning that the patient had only one kidney and hypertensive disease, interruption by subtotal hysterectomy was decided upon. In spite of this precautionary measure, her hypertension increased and several readings of 260 mm. of mercury systolic over 160 mm. of mercury diastolic pressures were observed. Finally on April 30, 1944, 2 years following the interruption of her third pregnancy, the patient died suddenly with convulsive seizures and uremia. At autopsy, generalized arterio and arteriolosclerosis with marked arterio and arteriolosclerotic nephritis of the left kidney was present. The heart showed dilatation and hypertrophy of the left ventricle.

This case illustrates the difficulties one can have if the unilateral pelvic ectopic kidney is complicated by other abnormalities of pregnancy or constitutional diseases.

The case for unilateral nephrectomy in the treatment of hypertensive disease is not as strongly advocated today as in 1940. Goldring and Chasis (96) feel that while an occasional effect may have resulted, the variable and often unpredictable course of the blood pressure is of such magnitude that acceptance of this therapeutic procedure must remain tentative. Each case of unilateral pelvic ectopic kidney may need special attention. The kidney itself need not be feared unless some specific disease process is present in the kidney, in which case the same treatment is necessary as though the kidney were in its normal location.

DIAGNOSIS AND TREATMENT

Bell (76) describes the ectopic kidney as being subject to all diseases to which the normal kidney is liable with no increased incidence of any lesion except hydronephrosis and pyelonephritis. Pain is the usual presenting complaint in the non-pregnant cases of ectopic kidney, usually of the back or abdominal type of pain radiating to the hips and thighs. This usually accompanies the disease processes of hydronephrosis and pyelonephritis. Sometimes pressure on neighboring structures, such as the bladder, may produce hematuria and pyuria. Gutier-

rez (79) emphasized a symptom complex in horseshoe kidneys, consisting of pain about the epigastrium or umbilical region, history of chronic constipation with or without gastro-intestinal disturbances, and also urinary disturbances with early signs of chronic nephritis. Gutierrez (79) believed that the great majority of horseshoe kidneys are diseased but Bell (76) is not able to support this view-point. R. Bell (101) sent a questionnaire to members of the American Urological Association on the subject of horseshoe kidney and pregnancy. He received 286 replies. In this group, 96 women with horseshoe kidney had normal uneventful pregnancies. Forty-nine mothers went to full term but had some complication of pregnancy. Eight cases had labor induced. To the question "Do you consider horseshoe kidney a contraindication to pregnancy?" the vote was yes, 23; no, 117; and no opinion, 139.

In Thompson and Pace's (58) series of 88 patients with ectopic kidney 29 or 32.9 per cent suffered from recurrent attacks of pain. They felt that this was due to improper drainage of urine through the ureteropelvic juncture because of anomalous blood vessels and constricting bands of capsular and peripelvic tissue. These authors also pointed out that the pain in pelvic ectopic kidney would not be necessarily in the lumbar region but may be of a bizarre nature such as in one of their patients, a boxer by profession, who noted an indescribable sensation low in the abdomen whenever he skipped rope.

Since many patients with pelvic ectopic kidneys do not have symptoms, the diagnosis during pregnancy will depend largely on thorough pelvic examination in the early months of pregnancy. If pelvic masses or urinary symptoms are present a complete urological survey of the patient including urography should be carried out. Unless the obstetrician has in mind the possibility of ectopic pelvic kidney very few cases will be diagnosed until the time of labor and delivery. Of 91 cases in the literature including 14 of the present study, on which accurate histories are available, the time of diagnosis in relation to the pregnancy may be summarized as follows:

Before pregnancy.....	4 cases	(4.39%)
During pregnancy.....	24 cases	(26.36%)
During labor.....	17 cases	(18.68%)
Immediate or late puerperium.....	8 cases	(8.79%)
Interval between pregnancies.....	8 cases	(8.79%)
Years after last pregnancy.....	23 cases	(25.27%)
At autopsy.....	7 cases	(7.69%)
Total.....	91 cases	

It is notable that only 4.3% of the cases were diagnosed before pregnancy; while 26% were diagnosed by astute examiners during the pregnancy. Many of the cases diagnosed during pregnancy were often seen during the second, third or fourth pregnancy and the examiner had some history of either difficult labors or urinary tract symptoms following previous deliveries. Approximately 30 per cent of the cases were diagnosed years after the pregnancy or were discovered at autopsy.

Of the 24 cases diagnosed during pregnancy, 4 were originally confused with ectopic pregnancy. Four other cases were called ovarian cyst. Approximately six cases had peculiar sacral, lumbosacral or "bearing down" type of pain as the initial symptom. The remaining ten cases were picked up by routine pelvic examination.

Seventeen cases were diagnosed during labor. Fourteen had painful and protracted labors which demanded further examination. In 3 cases the failure of the head to engage during active labor was the clinical point which attracted the attention of the examining physician.

Ectopic kidney in the non-pregnant patient usually requires no therapy until symptoms are present which have definite underlying pathological changes. The experience of Thompson and Pace (58) would justify this attitude. In their series of 88 clinical cases treatment was confined to simple therapy of pyelonephritis. Twenty-one surgical procedures were carried out, but in many instances normal kidneys were removed. Such surgical procedures as treatment of urinary tract fistulas, neoplasms, tuberculosis, atrophy of the kidney, hydronephrosis, or removal of stones may be entirely justified in both non-pregnant and pregnant individuals. These decisions should be wisely made by a competent urologist in consultation with the obstetrician.

In 91 cases where data are available the following surgical procedures have been carried out.

Sterilization.....	6 cases
Nephrectomy during pregnancy.....	5 cases
Nephrectomy after pregnancy.....	5 cases
Cesarean hysterectomy.....	4 cases
Puncture of pyonephrosis and hydronephrosis.....	3 cases

The decision as to the optimum type of delivery for the patient with labor complicated by pelvic ectopic kidney anomalies is not difficult at the present time in contrast to previous decades. The judicious use of cesarean section can be employed in specific dystocia problems in which the pelvic kidney plays a major role. If the 182 full term deliveries reported in the previous literature are added to the 27 full term deliveries of the present study, 209 full term infants have been delivered in the following manner with their respective fetal mortality rates:

<i>Method of delivery</i>	<i>Cases</i>	<i>Fetal deaths (per cent)</i>
Spontaneous.....	153	13 (8.4%)
Forceps.....	6	3 (50%)
Breech.....	11	5 (45.4%)
Version and extraction.....	5	4 (80%)
Cesarean section.....	32	3 (9.3%)
Craniotomy.....	2	2
Total.....	209	30

From the above tabulation it is apparent that a simple spontaneous delivery has about the same fetal mortality (8.4%) as cesarean section (9.3%), but if all

deliveries from below are included (177 cases) then 27 infants were lost, a fetal mortality of 15.2%. However, in 20 cases of full term deliveries in the authors' present study no fetal deaths occurred.

In 22 cases in which either bilateral pelvic ectopia with or without fusion or solitary kidney existed, in other words all of the patient's kidney function was located in the pelvis, the method of delivery was as follows:

<i>Method of delivery</i>	<i>Cases</i>	<i>Fetal deaths</i>
Spontaneous.....	15	0
Forceps.....	1	0
Cesarean section.....	5	0

It is apparent that the method of delivery can be as successful either by vaginal delivery or by the abdominal route if wise obstetrical decisions are made. Most cases of unilateral ectopic pelvic kidneys associated with pregnancy will deliver spontaneously provided the patient has an adequate pelvic capacity. This point should be checked not only by thorough clinical measurements but also by accurate x-ray pelvimetry. With adequate measurements of diameters of inlet, midplane, and outlet planes of the true pelvis, the average sized child and normal sized kidney will compensate in the available pelvic volume. This mechanism was readily demonstrated in Case 1 of the illustrative cases (Figure 3). Frequent rectal and sterile vaginal examinations should be made during the course of labor to ascertain whether or not the kidney is being impacted against the sacrum as the baby's head advances (Fig. 3). As long as the kidney possesses the mobility which was present at the onset of labor, it is apparent that the organ is not being subjected to abnormal pressure, which would in turn impede the forward progress or descent of the fetal head or injure the kidney parenchyma.

With bilateral pelvic ectopic kidney or solitary kidney, the obstetrician must remember that only 15 cases have been described in the world's literature. Therefore, although 16 of 22 full term birth cases have delivered of these women vaginally, no chances should be taken. If vaginal delivery is decided upon in this type of pelvic renal ectopia the patient should make constant progress during her labor. Any abnormality, such as unengaged head at onset of labor, failure of hourly progress in descent, with progressive dilatation and effacement of the cervix, abnormal contraction patterns should be carefully evaluated and abdominal delivery considered.

In conjunction with the urologist, chemotherapy should be instituted for urinary infections, with dilatation and surgical removal of calculi in an effort to promote better renal drainage especially in those cases with hydronephrosis. In spite of these measures, the urologist in a few cases may have to advise nephrectomy, if necessary, even during pregnancy.

Crabtree, Prather, and Prien (102), and Everett (77) have demonstrated that women with pre-existent urinary tract obstructive disease who have had pyelonephritis during their first pregnancy often have a severe renal injury in subsequent gestations, although the clinical manifestations may be relatively mild in character.

One of the most important points to be brought out in this review is the danger of removing an unidentified pelvic mass either by the obstetrician at the time of cesarean section, or at subsequent laparotomy, only to find out that the removed tumor is a kidney. Foley and Wilmer (103) in a discussion on the surgery of unilateral fused kidney found 5 cases in the literature in which inadvertent removal of the whole fused renal mass was, of course, followed by immediate death. Young (104) also cites 12 deaths following nephrectomy performed on solitary single kidneys.

Some of these patients after nephrectomy or with single solitary kidneys must be considered comparable with the lone kidney cases in pregnancy described by Mathews (105), Prather and Crabtree (106). Prather and Crabtree (106) reviewed the literature up to 1934 in which 396 pregnancies in 296 nephrectomized

TABLE X

Summary of the Maternal and Fetal Mortality of Cases of Pelvic Ectopic Kidney Anomalies Associated with Pregnancy in the Literature (1828-1948) and in the Present Study

	PREVIOUS LITERATURE	PRESENT STUDY			TOTAL
		Delivered at J. H. H.	Delivered elsewhere	Total	
Number of mothers.....	98	7	7	14	112
Maternal deaths.....	10 (10.2%)	0	0	0	10 (8.9%)
Pregnancies.....	226	18	22	40	266
Abortions.....	35 (15.4%)	5	7	12 (30%)	47 (17.6%)
Premature infants.....	9 (3.9%)	0	1	1	10 (3.7%)
Deaths—prematures.....	4 (44.4%)	0	1	1	5
Full term infants.....	182	13	14	27	209
Deaths—infants (full term).....	28 (15.3%)	0	2	2 (7.4%)	30 (14.3%)
Deaths—infants (viable).....	32 (16.7%)	0	3	3 (10.3%)	35 (15.9%)
Total fetal loss (including abortion).....	67 (29.6%)	5	10	15 (37.3%)	82 (30.8%)

women were included. Complications included: miscarriage 8%, toxemias 2.7%, and four deaths (1.4%). The deaths were due to eclampsia, (one case) and uremia (3 cases). Interruption of pregnancy was deemed necessary in 11.5%. Of 135 pregnancies with a known outcome, the fetuses were born alive and healthy, while in 20 or 14.9%, the babies were lost through miscarriage or stillbirth.

DISCUSSION

Only a few of the major points regarding the subject of ectopic pelvic kidney anomalies associated with pregnancy and labor will be discussed. In Table X a summary of maternal and fetal mortality of the previous literature including the 14 cases of the present study is presented. If the 14 cases of the present study are included there are now approximately 112 cases of pelvic ectopic kidney associated with pregnancy and labor reported in the world literature. Ten deaths have

deliveries from below are included (177 cases) then 27 infants were lost, a fetal mortality of 15.2%. However, in 20 cases of full term deliveries in the authors' present study no fetal deaths occurred.

In 22 cases in which either bilateral pelvic ectopia with or without fusion or solitary kidney existed, in other words all of the patient's kidney function was located in the pelvis, the method of delivery was as follows:

<i>Method of delivery</i>	<i>Cases</i>	<i>Fetal deaths</i>
Spontaneous.....	15	0
Forceps.....	1	0
Cesarean section.....	5	0

It is apparent that the method of delivery can be as successful either by vaginal delivery or by the abdominal route if wise obstetrical decisions are made. Most cases of unilateral ectopic pelvic kidneys associated with pregnancy will deliver spontaneously provided the patient has an adequate pelvic capacity. This point should be checked not only by thorough clinical measurements but also by accurate x-ray pelvimetry. With adequate measurements of diameters of inlet, midplane, and outlet planes of the true pelvis, the average sized child and normal sized kidney will compensate in the available pelvic volume. This mechanism was readily demonstrated in Case 1 of the illustrative cases (Figure 3). Frequent rectal and sterile vaginal examinations should be made during the course of labor to ascertain whether or not the kidney is being impacted against the sacrum as the baby's head advances (Fig. 3). As long as the kidney possesses the mobility which was present at the onset of labor, it is apparent that the organ is not being subjected to abnormal pressure, which would in turn impede the forward progress or descent of the fetal head or injure the kidney parenchyma.

With bilateral pelvic ectopic kidney or solitary kidney, the obstetrician must remember that only 15 cases have been described in the world's literature. Therefore, although 16 of 22 full term birth cases have delivered of these women vaginally, no chances should be taken. If vaginal delivery is decided upon in this type of pelvic renal ectopia the patient should make constant progress during her labor. Any abnormality, such as unengaged head at onset of labor, failure of hourly progress in descent, with progressive dilatation and effacement of the cervix, abnormal contraction patterns should be carefully evaluated and abdominal delivery considered.

In conjunction with the urologist, chemotherapy should be instituted for urinary infections, with dilatation and surgical removal of calculi in an effort to promote better renal drainage especially in those cases with hydronephrosis. In spite of these measures, the urologist in a few cases may have to advise nephrectomy, if necessary, even during pregnancy.

Crabtree, Prather, and Prien (102), and Everett (77) have demonstrated that women with pre-existent urinary tract obstructive disease who have had pyelonephritis during their first pregnancy often have a severe renal injury in subsequent gestations, although the clinical manifestations may be relatively mild in character.

additional cases observed in The Johns Hopkins Hospital during the years 1927 to 1948. The total number of pregnancies in the 98 mothers was 226, with an incidence of abortion of 15.4%, and a gross fetal mortality rate of 16.7 per cent. The fetal mortality rate for full term infants was 15.3% and the maternal mortality was 10.2%. Of the 14 patients in the present study, no mothers were lost and of 40 pregnancies, 12 ended in abortions, one in premature delivery, which infant died, and 27 full term infants with two infants (7.4%) dead. If the 14 cases of the present study are added to the 98 cases in the literature, a total of 112 cases of ectopic pelvic kidney anomalies associated with 209 full term deliveries have been recorded. Thirty infants died, a fetal mortality of 14.3%.

The method of delivery in 209 full term deliveries was spontaneous in 153 (73.2%), cesarean section in 32 (17%), forceps, 6 cases; breech in 11 cases; version and extraction in 5 cases; and craniotomy in 2 cases. The fetal mortality was 8.4% for spontaneous delivery as compared to 9.3% for cesarean section.

Unilateral ectopic pelvic kidneys occurred once in 4,886 pregnant women while bilateral pelvic kidney occurred only once in 34,206 deliveries.

Various types of ectopic pelvic kidney anomalies associated with pregnancy may be summarized as follows:

- (1) Simple unilateral pelvic renal ectopia, 97 cases in which 79% have left kidneys and 21% right kidneys
- (2) Bilateral pelvic renal ectopia, with or without fusion, 10 cases
- (3) Solitary pelvic kidneys, 5 cases

A discussion of the embryology, anatomy, symptomatology, diagnosis and treatment was presented.

The diagnosis and treatment during pregnancy depends upon thorough pelvic examination and investigation of pelvic masses. Such patients should be submitted to complete urologic investigation, including urography. X-ray pelvimetry is imperative to decide which patients have an adequate pelvic capacity for both kidney and the passage of the fetal head. The labor must be of an ideal type and continuous progress made, checked carefully by repeated vaginal examinations. During the labor the kidneys which possess any degree of mobility tend to rise out of the pelvis as the fetal head advances. Most women with ectopic pelvic kidneys may be delivered vaginally, but if all the renal tissue lies in the pelvis, such as bilateral pelvic renal ectopia, or solitary kidneys, the wiser method of delivery would be elective cesarean section.

Pelvic ectopic kidney per se does not constitute an indication for interruption of pregnancy or sterilization. However, with supervening disease, such as intractable pyelitis, tuberculosis, hydronephrosis, neoplasm or toxemia, such procedures may be advisable.

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occurred, a maternal mortality of 8.9 per cent. It should be pointed out, however, that no maternal death has been reported since 1927, and therefore, in the last 62 cases (inclusive of the present study) no difficulties regarding the maternal outcome have occurred. A total of 209 full term deliveries with 30 deaths or a fetal mortality of 14.3% is also recorded. This is a rather high fetal loss of full term babies but as shown in Table X, of 7 mothers who delivered 13 full term babies on the Obstetrical Service of the Johns Hopkins Hospital, no fetal deaths occurred.

Numerous variations of ectopic pelvic kidney anomalies have been reported and with the cases of the present study may be divided as follows:

I. Simple unilateral pelvic ectopia.....	97 cases
(a) Right kidney ectopia.....	16 (21%)
(b) Left kidney ectopia.....	60 (79%)
(c) Unknown.....	21
Total.....	97*
II. Bilateral pelvic kidney without fusion.....	4 cases
III. Bilateral pelvic kidney with fusion.....	6 cases
(a) Horseshoe kidney.....	4 cases
(b) Fused kidney.....	2 cases
IV. Solitary pelvic kidney.....	5 cases
Total.....	112 cases

* Five complicated by hydronephrosis.

Ninety-seven (86.5%) of the 112 cases were of the unilateral pelvic renal ectopia and 15 cases (13.5%) were varieties of bilateral or solitary pelvic ectopia of the kidney.

Spontaneous delivery in 153 full term deliveries carried a fetal loss of 8.4 per cent and in 32 infants delivered by cesarean section the fetal mortality was 9.3 per cent. It was apparent, however, that cesarean section was often delayed and frequently used in desperate attempts to secure a live infant after a protracted labor. It is obvious that a lower fetal mortality rate could be secured by more careful selection in those cases developing dystocia. The obstetrician must submit women with pelvic ectopic renal anomalies to vaginal delivery under ideal conditions utilizing abdominal delivery before fetal embarrassment takes place. Each case must have individual treatment. Chemotherapy must be used when indicated and every effort made to protect the ectopic kidney from infection. Urologic consultation should be had both during the pregnancy and puerperium. Modern therapy for dystocia, chemotherapy, x-ray pelvimetry, offer these women a much better outlook today than in the past. There is very little indication for sterilization or interruption of pregnancy in this condition unless other intervening diseases such as intractable pyelitis, hydronephrosis, tuberculosis, neoplasm or toxemia of pregnancy should occur simultaneously.

SUMMARY

This study included a review of 98 cases of pregnancy associated with pelvic ectopic kidney anomalies reported previously in the world's literature, and 14

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Obstetrics

PHYSIOLOGY OF PREGNANCY, LABOR AND PUERPERIUM

PHYSIOLOGY OF HUMAN CONCEPTION

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New England J. Med., 240: 804, 1949

It is unknown whether in the human ovary, all primitive ova are present at birth or whether new ones are formed from time to time. It is known that oogenesis continues in the rabbit and in the mouse.

The primordial oocyte becomes invested by several layers of granulosa cells: the adjacent connective tissue develops the theca interna, the latter secretes estrogen, empowering the granulosa layer to produce fluid. After preliminary conditioning by estrogen, the follicle responds to FSH. The follicle grows, with increasingly large amounts of estrogen and progesterone being secreted by the theca. The increasing estrogen causes the pituitary to diminish its production of FSH and produce more LH. This, in turn, results in an increased production of progesterone by the follicles. Meanwhile, the ovum has matured. The follicle ruptures and luteinization continues. More progesterone, as well as estrogen, is secreted. LH and its successor, the luteotropic hormone, acquire ascendancy and establish the corpus luteum. For about 10 days this produces increasing amounts of estrogen and progesterone. After the first week, it starts morphologic regression, having lost susceptibility to pituitary gonadotropins. It can, however, be revived by chorionic hormone. Only one follicle matures because in the human subject there is just enough LH in cooperation with FSH to evoke effective amount of progesterone and estrogen in only the most receptive follicle.

The accumulation of liquor folliculi increases the internal pressure; the whole growing graafian unit moves toward the surface. The continuity of the surface layers is broken, and the fluid and ovum escape. The chance of conception in human beings is exceedingly slight, if the nearest preceding coitus occurs more than 48 hours before ovulation, and the first succeeding, more than 12 hours after escape of the egg. Miosis, the process of diminution of chromosomes, is terminated in the tube 24 hours after ovulation. More chromosomes, to complete the species number, must soon be added. If ova approaching deacease, become activated, or if an aged sperm succeeds in fertilizing an ovum, the resultant conceptus is likely to be defective. Ovulation is the result of interplay among many complicated agents. No specific test has ever definitely indicated the exact time of ovulation. However, human ovulation occurs about 14 days before the first day of normal menstruation. The diphasic basal temperature curve, occurring in

normally menstruating women, may be related to ovulation. The increase in temperature is a function of progesterone. The day of the last lowest temperature from which it rises to stay permanently at a higher level, is taken to be the day of the ovulation phase. In most women, this assumed ovulation phase usually lies within 14 ± 2 days before menstruation.

The tubal fimbriae vary widely among women. Some consist of short and closely approximated growths of ciliated epithelium on a narrow flat collar of muscular connective tissue surrounding the ostium. Sometimes the flared end of the tube is found to have a long fringe that may extend outward to a radius of 2 cm. Modification of the ideal wider collar may be very significant to fertility. As ovulation approaches, the fimbria tends to engross the ovary in a curved, fan-shaped envelope. Motion of the cilia favors the entrapment of the ovum in the ampulla. There is little increase in the bulk of the ovum up to the 4-cell stage. Growth beyond this level takes place in the uterus. Tubal fluid may be a substrate delicately adjusted for the fertilization process and as a nutrient media for ova. Sojourn in the tube lasts not more than 4 to 5 days. Transportation of the ovum through the tube is effected by the ciliated endosalpinx and the peristalsis of the myosalpinx. There is reason to suspect that, at least in the rabbit, tubal fluid supplies an enzyme system favoring penetration of the sperm into the ova.

The conceptus, in the uterus, differentiates into 2 kinds of tissue. One develops into the embryo proper; the other is the trophoblast. It forages its way into the maternal vessels. While struggling on toward the maternal blood, the trophoblast is nourished by contributions from intercellular fluid. Whatever the food material is, its presence is induced by progesterone and estrogen from the corpus luteum. On the 7th day, the conceptus is barely imbedded, villi are not recognizable until it is 14 days old. During the week intervening, the corpus luteum is maintained by a gonadotrophin secreted by the trophoblast. The continuance of luteal activity substantiates the decidua. Later, the trophoblast takes over the work of the corpus luteum (on about the 25th day in the monkey) and secretes its own progesterone and estrogen. It is possible that glycogen or some easily utilizable glucoside secreted by the endometrium maintains the spermatozoa in their passage through the uterus.

Stretching of the vagina as occurs during coitus, brings the cervix into the axis of the vagina. The cervix produces a quantity of favorable fluid which, mixing with the ejaculate, maintains continuity through the canal with the fluid in the fundus. Throughout the phase of ovulation, the cervical secretion is plentiful, clear, alkaline, and easily penetrable to spermatozoa.

Spermatozoa are produced continuously through adult life by the germinal epithelium lining the seminiferous tubules. They are moved into the epididymis where some obscure maturing process takes place. In the vas, the column moves still onward. Those in the vas spill over to the posterior urethra and are washed out in the urine, but a large part of the whole column is ejected in the first stage of ejaculation. Within a split section of their arrival in the posterior urethra, the sperm are joined by a little secretion from the simultaneously contracting

prostate, and this mixture, made up largely of spermatozoa, is propelled to the cervical os. The total ejaculate varies from 3 to 9 cc. and contains about 500,000,000 spermatozoa. The respective characteristic contents of the prostate, vesicles, and vasa are not reestablished within 2 to 4 days. A second ejaculation within hours of the first contains comparatively few spermatozoa and a diminished amount of fluid. The enzyme, hyaluronidase, may be a factor in denudation of the granulosa vestment of the ovum. It is possible that this, or its precursor, is derived from the secretions of the prostate and/or vesicles.

During coitus much of the cervical mucus is spread onto the vaginal wall. This mucus mixes with the seminal discharge and the spermatozoa are thus protected from the usual acidity of the vaginal fluid. Female orgasm is very poorly understood, but conception is easy without it. After coitus, some of the ejaculate is absorbed by the vaginal epithelium; still other portions are extruded. Within 4 hours all spermatozoa remaining in the vagina probably die, because of reestablishment of the vaginal acidity.

Several hundred thousand sperm reach the cervix. Of these, tens of thousands migrate into the fundus, and a few thousand enter the tube. Probably not more than a few hundred reach the ampulla to meet the ovum. The cervical mucus at ovulation time offers a favorable substrate for spermatozoa. The spermatozoa swim through the tube in the direction opposite that produced by the ciliary motion; they are very large and strong in comparison to the force of the ciliary current.

The ovum encounters a few spermatozoa in the ampulla of the tube. Denudation of the granulosa and pellucid layers is desirable. These layers are held together by a glucoside called hyaluronic acid, which may be dispersed by the hyaluronidase present in sperm. This is by no means a certainty. Mammalian eggs have been fertilized *in vitro* in only 2 species, the rabbit and the human being, and in only one medium, Ringer-Locke's solution.

(This is the clearest, succinct description of the sequence of events associated with conception with which I am acquainted. To any one engaged in the teaching of obstetrics, the article should prove an invaluable aid as a concise reminder of the essential facts which the student should know; and in addition, it provides authoritative statements on many moot questions. The paper gains additional significance when it is recalled that Dr. Rock has himself made many important contributions to this obscure field.—Ed.)

VASCULAR CHANGES OF THE SKIN IN PREGNANCY—VASCULAR SPIDERS AND PALMAR ERYTHEMA

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Surg., Gynec. & Obst., 88: 739, 1949

Although American textbooks on obstetrics do not mention them, there are scattered references in medical writings to vascular spiders and palmar erythema as banal complications of pregnancy which tend to clear up following delivery. The vascular spider has been called by many names; it has been designated nevus, angioma, and telangiectasis. Three features characterize the usual variety, a body, legs, and surrounding erythema. A central point or eminence constitutes the body of the spider, and in small lesions this may be the only abnormality. In large lesions, it may project one or more millimeters above the level of the surrounding skin surface, and if of sufficient size, its pulsations may be felt. Branching legs or radicles come away from the body and decrease in size as the periphery is reached. The temperature over a vascular spider is higher than that of the surrounding skin because of the local increase in arterial blood, and fiery red color is characteristic. Blood flows from the body toward the periphery as may be seen in the refilling of a spider following its obliteration by pressure. There is a predilection for distribution over the upper parts of the body with the face, neck, upper chest, and arms frequently affected. (See Fig. 1.)

Palmar erythema may occur in 2 distinct forms during pregnancy. The first variety is similar to the "liver palms" of chronic hepatic disease. It begins as a diffuse redness prominent in the proximal part of the hypothenar eminence. In the advanced stages, the parts of the palm between the metacarpophalangeal joints develop red spots and the palmar pads of the finger tips become red. The other variety consists of a diffuse mottled erythema involving the entire palmar surface. There is a trend for redness to increase in intensity as pregnancy progresses. These vascular changes of the hand have no regular relation to edema of the hands.

Vascular spiders were found in 321 or 66.6% of the 484 white women observed, and in 87 or 11.4% of the 759 negro women at some time during pregnancy. Only such lesions as could be recorded by ordinary black and white photography were included as spiders in the data. Palmar erythema was observed in a total of 300, or 62.5%, of the white women and 263, or 35%, of the negro women in this study. Palmar erythema was almost 3 times as common as vascular spiders in negro women, while there was only a slight difference in the incidence of vascular spiders and palmar erythema in white women. The most probable cause is the variation in skin pigment which is much less deep in the palms than in other areas of skin of negro women. Palmar erythema was observed in 67% of

prostate, and this mixture, made up largely of spermatozoa, is propelled to the cervical os. The total ejaculate varies from 3 to 9 cc. and contains about 500,000,000 spermatozoa. The respective characteristic contents of the prostate, vesicles, and vasa are not reestablished within 2 to 4 days. A second ejaculation within hours of the first contains comparatively few spermatozoa and a diminished amount of fluid. The enzyme, hyaluronidase, may be a factor in denudation of the granulosa vestment of the ovum. It is possible that this, or its precursor, is derived from the secretions of the prostate and/or vesicles.

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the white women who had vascular spiders. Vascular spiders were observed in 71% of the white women who exhibited palmar erythema. Thus if either type of vascular change was found, the other was about twice as likely to be present as to be absent. This suggests but does not prove that there may be a common cause.

Vascular spiders or palmar erythema may be found in normal nonpregnant women. Observations indicate that a vascular spider may be found in about 10% of white women who have borne children. In a study made by one of the authors during a nutrition survey of American troops in various islands in the Pacific,

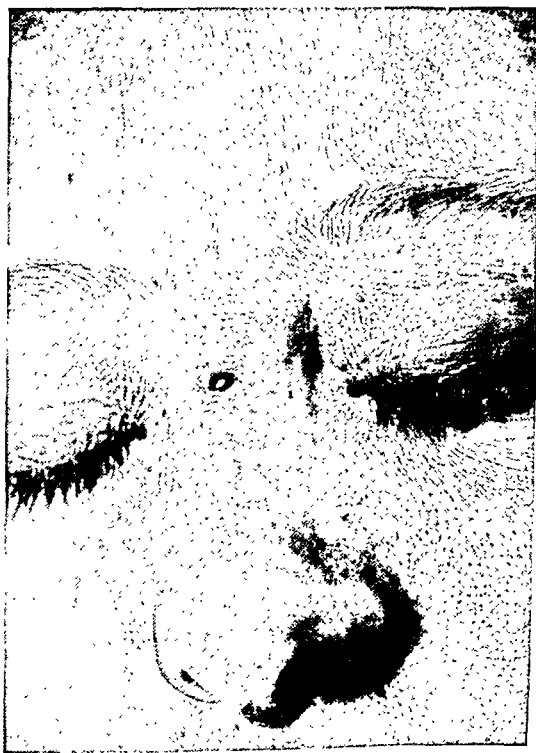


FIG. 1. Example of vascular spider (courtesy Drs. of Bean, Cogswell, Dexter and Embick)

it was found that vascular spiders were seen in 14.9% of the white and in none of the negro soldiers. Even with these as a base line, there is a marked and consistent increase in the number of women with vascular spiders and in the number of spiders per woman from the 2nd or 3rd month of pregnancy until term. At this time there is a complete disappearance of many so that by the 7th week after childbirth, the number approaches that found in control groups. Subsequently there is a further decrease which apparently continues slowly so long as another pregnancy does not occur.

These studies have established the surprising frequency of the vascular spider and palmar erythema as banal accompaniments of normal pregnancy. The authors advance the hypothesis that these phenomena may be caused by hormones, and implicate the estrogenic substances in particular. The facts recorded should be known to obstetricians, if only for the occasional comfort they bring to women whose worry about such blemishes may add its needless burden to the trials of pregnancy.

(Further information about vascular spiders will be found in Bean's extensive review of this subject, "The Cutaneous Arterial Spider: A Survey," published in *Medicine*, 1945, 24: 243. In that paper Bean points out that these spiders may occur in the following classes of persons: (1) subjects with liver disease; (2) pregnant women; (3) persons with deficiency disease caused by lack of the B-complex vitamins; and (4) normal persons. The observations which Bean and his associates have recorded demonstrate that the spider tends to occur as a complication of hepatic disorders when they are long and severe, but that no common sign or functional variation parallels its fluctuations, foreshadows its advent or anticipates its regression. In pregnancy spiders usually appear anywhere from the second to the fifth month, and in most cases fade abruptly during the period of uterine involution. They appear to be directly associated with deficiency diseases only when the liver is deranged. In many instances their occurrence appears to be fortuitous. In the presumably normal persons so affected they are governed by forces which are altogether obscure.

As stated in the last paragraph of the abstract, the hypothesis has been advanced that a cause of this alteration in the small arteries of the skin is an increase or qualitative change in circulating estrogens or hormones of related chemical structure, a change that is normal in pregnancy, but pathological in hepatic disorders in which the liver fails in its function of keeping the 17-ketosteroids in balance and at a proper level. In speculating upon the possible role which the estrogenic hormone may play in the formation of vascular spiders, Bean points out that the acute action of estrogens upon the minute vessels of the ear of ovariectomized rabbits has been reported by Reynolds and Foster to cause dilatation (*J. Pharmacol. & Exper. Therap.*, 1940, 68: 173). In his opinion it is not unlikely that a protracted action might affect the blood vessels throughout the body as well as those of the female genital tract which have been investigated extensively. Thus the studies of Bartelmez and Markee on the spiral arteries in the endometrium suggest at least a morphological similarity to the cutaneous arterial spider which Bean and his associates have found to be a smaller coiled end-artery in the subcutaneous tissue. A study of a serially cut vascular spider indicates close similarity to the endometrial end-artery pictured in a reconstruction by Jones and Brewer (*Am. J. Obst. & Gynec.*, 1939, 38: 839). An additional suggestion presented itself when Bean and his group found that during the menstrual cycle there were visible changes in the arterial spider in the skin of certain normal non-pregnant women who had acquired the condition during gestation.

The differentiation of Osler's disease (hereditary hemorrhagic telangiectasia) from the vascular spider has been considered by Bean in detail. The vascular aberration in Osler's disease is ubiquitous in distribution, pervading the inner reaches of the body as well as its mucous and cutaneous surfaces; it gives rise to repeated hemorrhages from trivial trauma; having once become manifest it does not regress; and it is inherited as a dominant trait. It is usual for a large number of lesions to occur in any victim of this disease. In size and shape telangiectasis differs from the vascular spider. It is smaller, punctate, often of firm consistency, purplish in color, and only rarely is it pulsating. Although the vessels carry arterial blood, the lesion is a tangle of thin walled, dilated, contorted vessels near the surface, and is not conspicuously warmer than adjacent skin. Contrariwise, the vascular spider has a special predilection for the upper parts of the body, particularly the blush area, but may occur in mucous surfaces; it may bleed, but this has occurred in fewer than 5 per

cent of Bean's subjects. The role of heredity is not certain, but a familial tendency is sure in many instances. Spiders have a most curious faculty of changing size, of appearing and disappearing, of coming in explosive eruptions and perhaps fading away almost as precipitously. The region encompassed by the vascular ramifications of the arterial spider is warmer than the adjacent skin and if the location is favorable and their size is large, spiders can be felt to pulsate. Many lesions are large, measuring in rare cases two or more inches in greatest diameter.

Although many questions about vascular spiders in pregnancy remain unanswered, the detailed description which the authors have presented of this cosmetic nuisance and its favorable prognosis will be welcome information to obstetricians everywhere.—Ed.)

THE UTILIZATION OF NICOTINIC ACID BY PREGNANT WOMEN

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J. Nutrition, 37: 393, 1949

The authors selected 3 groups of women for study: Group I consisted of 7 healthy primigravidae during the last 5 months of pregnancy; Group II included 42 clinic patients selected at random from the Chicago Lying-In Hospital; Group III included 12 non-pregnant women. The 7 subjects in Group I lived at home and ate self-selected diets. During each of the last 5 months of pregnancy, 7-day balance studies were made on all the patients. These studies included: (1) daily nicotinic acid intake, (2) urinary excretion of (a) the acid hydrolyzable fraction and (b) N'-methylnicotinamide. Concurrent with the study of the 2 groups of pregnant women, similar information was obtained on the 12 non-pregnant women.

There was considerable variation from month to month in the intake of nicotinic acid by various subjects in Group I. The average daily intake for the 5 subjects on unsupplemented dietaries ranged from 13.8 to 18.3 mgm. The average daily intake for all subjects was 19.7 mgm. The average daily excretion of the acid-hydrolyzable metabolites of nicotinic acid was 1.1 mgm. The average daily excretion of N'-methylnicotinamide for all subjects over the 5 month period was 13.8 mgm (expressed as nicotinic acid). The amount of N'-methylnicotinamide excreted by the 5 subjects on unsupplemented dietaries showed only slight relation to intake. In general there was a slight increase in excretion of the methylated derivatives with increased duration of pregnancy. Statistical analysis of the data showed that there is a real difference in the levels of excretion of N'-methylnicotinamide by primigravidae on unsupplemented dietary intake of nicotinic acid with progression of pregnancy.

Data obtained upon the 42 clinic patients indicated a more or less constant level of excretion of the methylated derivative regardless of intake. In the second group there was also an increase in level of excretion of N'-methylnicotinamide with increased duration of pregnancy. In the third, or non-pregnant group, the level of excretion of the methylated derivative was much lower than in the pregnant women.

The authors suggest that the observed increase in level of excretion of N'-methylnicotinamide during the last trimester of pregnancy might be attributed to an increase in the requirement of the maternal organism for Co-enzymes I and II, paralleling the increase in total body metabolism. This reasoning is based upon the assumption that the methylated derivative is a true metabolite of nicotinic acid.

EFFECT OF DIETHYLSTILBOESTROL ON URINARY EXCRETION OF PREGNANEDIOL AND ENDOGENOUS OESTROGEN DURING PREGNANCY

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Lancet, Lond., 1: 680, 1949

Smith et al. (Am. J. Obst. & Gynec., 51: 411, 1946) proposed giving diethylstilbestrol by mouth as a prophylactic to pregnant women with histories of repeated accidents in pregnancy. This proposal is based on the suppositions that many accidents of late pregnancy are referable to a deficiency in the secretion of progesterone and other sex steroids by the placenta, and that the secretion of these steroids can be stimulated with diethylstilbestrol.

The authors report the results of an investigation of the effect of diethylstilbestrol on the urinary excretion of pregnanediol during pregnancy; the urinary excretion of endogenous estrogen was also studied. One non-diabetic pregnant woman and 3 diabetic pregnant women were studied. Urinary pregnanediol was determined by the method of Sommerville et al. Total urinary endogenous estrogen was determined by the method of Stevenson and Marrian. Doses of diethylstilbestrol ranged from 25-50 mg. daily.

In every instance, the administration of diethylstilbestrol caused a sharp fall in the excretion of pregnanediol; after withdrawal of the estrogen, the excretion rose either immediately or after a short delay. The administration of diethylstilbestrol causes no gross change in the endogenous estrogens. Knowledge of the metabolism of progesterone is so incomplete that it should not be assumed that changes in the excretion of pregnanediol in the urine necessarily reflect changes in the secretion of endogenous progesterone.

(The authors of this paper are one of the most experienced groups of investigators in the field of endocrinology and their findings attest the conviction that our knowledge of hormonal physiology in pregnancy is in a very muddled state. In the article cited by Smith, Smith and Hurwitz, a chart of a patient is shown in which "the urinary excretion of pregnanediol rose steadily while diethylstilbestrol was being taken, and dropped precipitously each time it was omitted." Yet in the above investigation the administration of diethylstilbestrol in every instance caused a sharp fall in the excretion of pregnanediol; and after

withdrawal of the estrogen, the excretion rose either immediately or after a short delay. In other words, no two studies could be more contradictory. From a clinical viewpoint the administration of stilbestrol in cases of habitual abortion and in other complications of pregnancy, is based largely on the premise that it stimulates progesterone production; and otherwise, as far as I am aware, it would be without any established rationale. It is to be hoped, therefore, that the reason for this discrepancy can be elucidated in the immediate future so that the real truth about this important issue will at last be at hand.—Ed.)

MANAGEMENT OF NORMAL PREGNANCY, LABOR AND PUERPERIUM

PARTURITION FOLLOWING EARLY RUPTURE OF THE MEMBRANES, BOTH SPONTANEOUS AND ARTIFICIAL

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Ztschr. Geburtsh., 129: 3, 1948

Premature rupture of the membranes was formerly regarded as a serious complication: more recently, however, it has been viewed as a physiological variation. The older authors feel that the bag of waters favors dilatation of the cervix. In the absence of the amniotic sac, labor is slowed, and the incidence of infection is increased. Uterine inertia, intrapartum infection, and prolapse of the cord are alleged to be commoner following premature rupture of the membranes. Hence, an additional danger to the fetus is present.

The newer group feel that the process of delivery is, in general, shortened following premature rupture of the membranes. They deny the incidence of increased infection and prolongation of labor.

In a similar way, opinions are divided as to the advisability of artificial amniotomy prior to labor. The older school maintains that the bag of waters ideally should be preserved, at least until full dilatation. The other group, which includes some American authors (Guttmacher and Douglas, Jackson, and Wilson) have reported an early onset of labor and no prolongation of the normal duration of labor following artificial rupture of the membranes. In the material of numerous authors in this group, there has been no increase in fetal mortality.

Premature spontaneous rupture of the membranes is frequently associated with obstetrical abnormalities, such as malposition, prematurity, pelvic contraction and multiple pregnancy. Correction of the statistics relating to premature spontaneous rupture involved elimination of all prematures, transverses, breeches, multiple pregnancies, and pelvic contractions. The corrected statistics deal only with occiput presentation of full term and post term pregnancies in primiparas and multiparas. The station of the head, the dilatation of the cervix, and the amount of effacement at the time of spontaneous rupture are not included, because they were obviously unknown.

At first, the author employed artificial rupture of the membranes prior to the onset of labor only in multiparas with prolonged pregnancy. The results were so good that the method was applied to other obstetrical complications, such as toxemia. The results continued to be good, and the method was applied to full term multiparous pregnancies without special indication. Relatively recently, the method has been extended to primigravidas. Certain conditions have been required: all abnormal presentations, multiple pregnancies, and contracted pelves

are excluded. Moreover, the fetus must be mature. In multiparas, the cervix must admit the finger. In primiparas, the cervix must not only admit the finger, but must also be partially taken up.

Table I shows the latent period before onset of labor following premature rupture of the membranes. It was necessary, also, to correct the statistics for premature artificial rupture, because in the early portion of the series, all of the criteria enumerated above were not fulfilled. The difference in the latent period between the spontaneous and artificial group is doubtless due to the fact that the cervix must have been unfavorable in some of the former. There were 350 uncorrected cases among those with artificial rupture; 303 cases remained after correction. The total number of uncorrected cases among those with spontaneous rupture was 340; 230 remained after correction.

TABLE I
Duration of Latent Period (Average)

	PARITY	SPONTANEOUS RUPTURE	ARTIFICIAL RUPTURE
Uncorrected	Primiparas	12' 56"	6' 15"
	Multiparas	11' 18"	4' 58"
Corrected	Primiparas	7' 15"	4' 36"
	Multiparas	8' 1"	4' 18"

TABLE II
Duration of the First Stage

	PARITY	SPONTANEOUS RUPTURE	ARTIFICIAL RUPTURE
Uncorrected	Primiparas	7' 57"	8' 21"
	Multiparas	5' 12"	4' 23"
Corrected	Primiparas	7' 11"	6' 32"
	Multiparas	4' 44"	3' 38"

The latent period in the corrected series of spontaneous rupture was over 24 hours in only 12 cases and was never greater than 36 hours, except in one case which required cesarean section for primary inertia after 79 hours. Among the corrected artificially ruptured group, 119 had a latent period of one hour or less.

Table II shows the average duration of the first stage in the author's series. The duration of the first stage is quoted all the way from 6 to 18 hours in various textbooks. The great reduction observed in the present series is related to reduction of spasm of the internal os.

Table III shows the duration of the 2nd stage. The similarity of the 2 groups indicates that the difference between spontaneous and artificial rupture pertains mostly to the first stage, and is a function of the state of preparedness of the cervix at the time the membranes rupture. Again, the author's values for the

duration of the 2nd stage are significantly shorter than those quoted in the literature. In contrast, the duration of the 3rd stage in the author's series was not significantly different from the normal.

Table IV shows the total duration of labor in the author's series. These figures are significantly shorter than those given in the literature. The delay in delivery in the uncorrected series is traceable to the associated complications.

TABLE III
Duration of the Second Stage

	PARITY	SPONTANEOUS RUPTURE	ARTIFICIAL RUPTURE
		<i>min.</i>	<i>min.</i>
Uncorrected	Primiparas	52	54
	Multiparas	22	25
Corrected	Primiparas	49	52
	Multiparas	25	24

TABLE IV
Total Duration of Labor

	PARITY	SPONTANEOUS RUPTURE	ARTIFICIAL RUPTURE
Uncorrected	Primiparas	9' 8"	9' 33"
	Multiparas	5' 58"	5' 7"
Corrected	Primiparas	8' 21"	7' 43"
	Multiparas	5' 28"	4' 22"

TABLE V
Incidence of Obstetrical Complications

	PARITY	SPONTANEOUS RUPTURE	ARTIFICIAL RUPTURE
Uncorrected	Primiparas	12%	7.3%
	Multiparas	19	3.0
Corrected	Primiparas	8%	6.5%
	Multiparas	3.2%	1.2

Obstetrical complications were defined by the author as primary and secondary inertia, passage of meconium-stained fluid, slowing of the fetal heart, deep transverse arrest, and prolapse of the umbilical cord or small parts. Tables V and VI show the incidence of obstetrical complications and obstetrical operations in the author's series. Statements in the literature as to the frequency of complications following normal rupture of the membranes are so variable that an average value cannot be determined.

Complications of the 3rd stage were defined as including the necessity for

Credé's expression or manual removal of the placenta, and the presence of uterine atony. No complications whatever were observed in the corrected series of artificial ruptures. The incidence was 4.0 and 1.6% respectively in the spontaneous group.

Table VII shows the frequency of puerperal complications. These corrected values are again superior to those found in the literature. The reduction of puerperal fever is especially striking; this is probably because labor is so short that infected material has less time to ascend into the uterus.

The incidence of danger to the infant was not significantly increased. Asphyxia, slowing of the fetal heart, and passage of meconium were not increased. The overall fetal mortality for both types of rupture among the corrected cases was 0. Among the uncorrected cases, a total of 7 babies were lost in both groups out

TABLE VI
Incidence of Obstetrical Operations

	PARITY	SPONTANEOUS RUPTURE	ARTIFICIAL RUPTURE
Uncorrected	Primiparas	13.3%	7.3%
	Multiparas	20.0	3.0
Corrected	Primiparas	8.0%	5.5%
	Multiparas	1.6	0.6

TABLE VII
Frequency of Puerperal Complications

	PARITY	SPONTANEOUS RUPTURE	ARTIFICIAL RUPTURE
Uncorrected	Primiparas	15.9%	9.8%
	Multiparas	21.0	5.8
Corrected	Primiparas	12.0	6.4
	Multiparas	4.5	3.3

of 690. One child was prematurely born following version and extraction, another died after prolapse of the cord, and still another succumbed following intrapartum fever.

The maternal mortality in both corrected series was 0. The total number of maternal deaths in the series was 2. One woman died of overwhelming sepsis (presumably following a throat infection). The second patient died of puerperal sepsis on the 36th postpartum day.

The author concludes that premature artificial rupture of the membranes is a worthwhile procedure if the cervix is partially effaced and admits a finger. Under these conditions, the average duration of the latent period is 4 hours, the length of labor is shortened, there are fewer complications during and after labor, and the danger to the mother and child is not increased. Similar conditions obtain

following spontaneous premature rupture. Here, however, they are not so favorable, because the cervix may be less suitable when rupture occurs.

(Strangely enough, artificial rupture of the membranes was the favorite method of inducing labor prior to 1800, fell into disuse during the nineteenth and early twentieth centuries and was not restored to favor until around 1930. Just why the procedure was virtually abandoned during the nineteenth century and afterwards is not altogether clear but is presumably connected with two factors: (1) emphasis on the doctrine that the bag of waters is essential to physiologic dilatation of the cervix; and (2) the introduction about 1850 of bougies and bags which were long deemed the best instruments for inducing labor. The derogatory attitude long held toward artificial rupture of the membranes becomes understandable when it is recalled that "dry labor" used to be a bugbear which any obstetrician dreaded. This reaction to dry labor was dispelled by several papers appearing in the late twenties which demonstrated that premature spontaneous rupture of the membranes is not necessarily followed by prolonged labor and, provided that all else is normal, may actually expedite labor. One of the most important and influential of these articles was that of Margaret Schultz dealing with 604 cases of dry labor occurring in a series of 6,500 deliveries (9.3 per cent). She considered only those cases in which rupture of the membranes occurred prior to or at the onset of labor. The length of labor was shorter than the average for patients with intact membranes, the first stage being chiefly affected. The average of the first stage was 12.1 hours for primigravidae and 7.1 hours for multiparae, with second stages averaging 1.8 hours and 0.9 hours respectively (*Am. J. Obst. & Gynec.*, 1929, 17: 20). About the same time Morton showed that bags and bougies left much to be desired (*Am. J. Obst. & Gynec.*, 1929, 18: 849); and the way was opened for the studies mentioned in the above abstract which reinstated artificial rupture of the membranes.

It will be noted that Odenthal eliminates all abnormalities from his series, such as pelvic contraction and transverse and breech presentations. This is altogether correct in studying the intrinsic effect of rupture of the membranes on labor. On the other hand, this correction should serve to remind us that premature rupture of the membranes cannot always be regarded with equanimity and that in the three conditions mentioned it is an unfavorable sign. In pelvic contraction early rupture of the membranes suggests substantial disproportion. In breech presentation, it frequently presages slow cervical dilatation; while in transverse presentation premature rupture of the bag of waters is an extremely ominous sign being followed, indeed, by a fetal mortality which approximates 50 per cent if vaginal delivery is employed.—Ed.)

THE MEASUREMENT OF THE ANTERIOR OBSTETRICAL SAGITTAL DIAMETER

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West. J. Surg., 57: 245, 1949

Direct pelvimetry is being neglected. The first reason is the rapid development and progress in x-ray study of the pelvis. The second reason is that measurements of little or no consequence long have been emphasized, and points of great importance have been neglected. The elimination of all but the important diameters would cause attention to be directed to the ones that have definite prognostic value as far as labor and delivery are concerned.

The first of the important measurements is the conjugate of the inlet. Since a trial of labor for inlet contraction can be tried safely and without undue discomfort to the patient, the measurement finds its importance only in the detection of marked contraction. Means of prognosticating the course of labor in the midpelvis and at the outlet become much more important. Reliable guides to the midpelvis and outlet would enable one not only to foresee need for abdominal delivery earlier, but would eliminate many unnecessary sections.

The anterior obstetrical diameter is the distance from the midpoint of a line between the pubic rami where they diverge to a distance of 8 cm., to the upper border of the symphysis. The selection of the points at which the pubic rami diverge to a distance of 8 cm. is based on the observation that with an average sized baby, the skull touches the rami at these points; as the head extends, the line joining these 2 points acts as a fulcrum. As the anterior obstetrical sagittal measurement increases, difficulties in the midpelvis and at the outlet can be expected. A measurement of 7 to 9 cm. indicates no midpelvic or outlet problems. From 9 to 10.5 cm., these problems are minor; above 10.5, they become increasingly serious, and above 11.5, they usually result in abdominal delivery unless the fetus is very small.

To measure the anterior obstetrical sagittal diameter easily, an instrument similar to the Thoms' pelvimeter has been devised. The base is a fixed bar measuring 8 cm. with finger loops at both ends. One arm of a caliper is fixed at the midpoint of this bar and the other end of the caliper is movable. With the patient in lithotomy position, the point where the divergence of the pubic rami reaches 8 cm. is palpated with the thumbs inserted through the finger loops. The bar is held at this point and the tip of the movable arm of the caliper is brought down on the upper border of the symphysis; the measurement is then read off directly on the scale. The measurement can be done quickly and without discomfort to the patient. By using the diagonal conjugate and this measurement, x-ray pelvimetry will be unnecessary in many cases.

PATHOLOGY OF PREGNANCY

CEREBRAL COMPLICATIONS RESULTING FROM HYPERTENSION CAUSED BY VASOPRESSOR DRUGS IN OBSTETRICS

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New York State J. Med., 49: 1424, 1949

This report is intended as a caution against the inadvertent combination of vasopressor drugs in obstetrics. Ephedrine or similar drugs are commonly used in obstetrics nowadays because of the increasing application of caudal and spinal anesthesia. When these drugs are preceded or followed within a half hour by pituitary extract and/or ergonovine, the elevation of blood pressure may be marked and abrupt. The authors have observed a significant rise (between 50 to 100 mm. Hg systolic pressure) in 6 cesarean sections and 8 vaginal deliveries. One patient developed a hemiplegia.

Intrauterine injection of pituitary extract is practiced by some operators. Such an injection may be very similar to an intravenous injection. When the fetus and placenta are delivered and the uterus contracts, a significant quantity of blood is squeezed into the general circulation. This tends to cause an elevation of blood pressure. The episode of acute hypertension which results may be asymptomatic or manifested by severe acute headache.

Ergotrate, in itself, causes little or no rise in blood pressure when injected intravenously. The presence of ephedrine, however, permits intravenous ergotrate to cause a 60 mm. Hg rise in systolic pressure.

Treatment of the acute hypertension may include amyl nitrite, increased dosage of spinal anesthesia, or intravenous pentothal.

(The warning sounded in this article about the synergistic action of ephedrine and oxytocic drugs is timely and well substantiated. This is one reason why obstetricians and anesthesiologists, in the case of cesarean section at least, prefer to give the ephedrine 30 minutes before the spinal anesthesia is started; if this is done, the effect of the ephedrine has usually worn off by the time the pituitary extract or ergonovine is needed. However, in vaginal deliveries, this timing of the drugs is not always feasible and the danger of blood pressure elevation should be borne in mind especially in cases of toxemia.—Ed.)

A VARIANT OF THE HOFSTATTER-CULLEN SIGN IN INTRA-ABDOMINAL HEMORRHAGE FROM ECTOPIC PREGNANCY

With a Note on the Mechanism of Its Production

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New England J. Med., 240: 747, 1949

Ordinarily one thinks of Cullen's sign as the blue navel of ectopic pregnancy. The sign can be caused by intra-abdominal hemorrhage from any source. After ectopic pregnancy, the next most frequently reported cause is acute pancreatic necrosis. The mark may be red, purple, blue, green, tan, yellow or many colors. In the 70 occurrences that the authors have been able to trace, the location was most often at the umbilicus, but hernial sacs and old surgical scars are frequent sites.

Stabler (1934) reported a case in which there was a dark-purple mark 2 or 3 cm. downward and to the left of the umbilicus; a second circular blue mark in the midline a third of the distance from the umbilicus to the symphysis, and a third mark over the left external inguinal ring. He found no blood in the peritoneal tissues at the site of incision. The intraperitoneal hemorrhage was small, 90 to 120 cc.

Neumann's (1928) patient, with a large amount of partly clotted blood in the peritoneal cavity, on the 10th day after her first symptom, showed 2 non-umbilical ecchymoses. One was at the level, but to the left, of the umbilicus, the other was 2 or 3 cm. beneath it in the midline. One was green, and the other yellow-green.

The authors report a third case. The patient had 3 separate ecchymoses; a small irregular stain in the umbilicus and 2 larger circular stains, symmetrically located on either side of the umbilicus. Lines of varying intensity formed arcs of concentric circles, the common center of which was the umbilicus. The time of appearance of the sign is fixed as between 4 and 6 hours after syncope. The amount of blood, widely distributed throughout the peritoneal cavity and partly clotted, was 400 cc.

The location of the stains in these 3 cases, as well as the more ordinary localizations over hernias, in scars and at the umbilicus, suggests that the pigments that usually produce the phenomenon may reach their destination by following ordinary fascial planes and openings, rather than by depending upon exceptional lymphatic function or subvisible peritoneal apertures. There are major fascial gaps at the umbilicus, midline, and inguinal rings, and in hernias and scars; there are minor ones where vessels perforate the rectus sheath.

(Although Cullen's sign is valuable evidence of intraabdominal hemorrhage, it is rarely demonstrable, at least in my own experience. Thus, I have observed it only once in ectopic pregnancy and even in that case the coloring was so faint that a kodachrome photograph of the umbilical region failed to reproduce it.—Ed.)

OVARIAN PREGNANCY

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J. Michigan M. Soc., 48: 577, 1949

The authors review the literature and present a case which fulfills the criteria for a true ovarian pregnancy. The criteria (Spiegelberg) are: (1) the tube on the affected side is intact; (2) the fetal sac occupies the position of the ovary; (3) the sac is connected with the uterus by the utero-ovarian ligament; and (4) definite ovarian tissue is found in the sac wall.

The patient was a 31 year old white woman admitted with the complaint of vaginal bleeding of 4 weeks' duration. Her menstrual history was irregular, the last "regular" period being 4 months prior to admission. On physical examination there was tenderness to deep palpation in the right lower quadrant. Pelvic examination revealed the uterus to be anterior and of normal size. Tenderness was most marked on movement of the cervix. The right adnexa seemed prolapsed and thickened; the left seemed to present a tender mass encroaching the cul-de-sac. At this time, the impression was that of ectopic pregnancy, subacute pelvic inflammatory disease, or ovarian cyst. A Friedman test was reported positive. At laparotomy there was a large, soft necrotic mass occupying the entire posterior cul-de-sac. This mass was intimately connected to the right ovary; the tube and ovary on the left side appeared normal. There was no evidence of recent abortion from the tube, and the lumen was patent throughout. The right ovary appeared to be exploded in the middle, with just a shell remaining. The right ovary was removed; the cul-de-sac was cleaned of all necrotic debris, and the uterus suspended. The right tube appeared normal; the lumen was tested and found to be patent throughout. Microscopic examination showed involutional or compression atrophy of the ovary. There was no decidual reaction attached to the ovary. There was a separate mass with ovarian fragments showing a typical extrauterine pregnancy with trophoblastic decidua in contact with the ovary. There was one surviving chorionic stem.

X-RAY VISUALIZATION OF THE PLACENTA: EXPERIENCES WITH SOFT-TISSUE AND CYSTOGRAPHIC TECHNIQUES IN THE DIAGNOSIS OF PLACENTA PREVIA

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Am. J. Obst. & Gynec., 58: 15, 1949

The placenta can be visualized in soft-tissue x-ray films in over 90% of women in the 3rd trimester of pregnancy. At the Boston Lying-in Hospital, all cases of uterine bleeding and transverse or oblique presentation during the 3rd trimester have been studied by x-ray. X-ray visualization of the placenta has been attempted since 1930, using various methods. Radio-opaque media have been injected into the uterus, as well as the bladder. Soft-tissue films have been used by many authors. The reported success in placental localization varies between 85 and 97%.

At the Boston Lying-In Hospital, the technique for placentography is as follows: the KVP is varied between 75 and 82, depending upon the degree of obesity; 100 Ma. and an exposure time of 1-2 seconds; and a tube-film distance of 40 inches are used. No filters nor special equipment is necessary. The first film is taken with the patient lying on her side. If the first film does not show the placenta, the patient is placed on the other side, either with the transverse axis of the pelvis perpendicular to the table top or at some degree of obliquity to it, according to the findings in the first film. Since 85 to 90% of placentas lie either on the anterior or posterior wall of the uterus, the lateral film is usually sufficient. In some cases, a second film is taken with the patient lying flat on her back, allowing visualization of the placenta lying on one or the other lateral wall. In order to have the placenta show on the film, it is important to obtain an edge-wise view of its central vertical axis. If the presenting part overrides the inlet, the films may be taken in the standing position. In these cases, gravity will bring the presenting part downward to a closer approximation with the inlet. If the patient has a relaxed anterior abdominal wall and postural hyperextension of the lumbar spine, the head may override the symphysis. In such cases, standing cystograms are often taken.

Cystographic studies are done when the placenta is not adequately demonstrated by the soft-tissue technique or if the findings are suggestive but not diagnostic of placenta previa. One hundred to 200 cc. of 12.5% NaI is injected into the bladder; an AP film is then taken with the patient lying on her back. If the film is not conclusive, a lateral cystogram may be made. If these films are unsatisfactory, the views may be repeated with the patient standing. Injection of air into the sigmoid may also be of assistance.

This study covers 488 x-rays taken on patients in the 3rd trimester of pregnancy. Readable films were obtained on 474 women. In this latter group, the

correct diagnosis of presence or absence of placenta previa was made in 98.1% of the cases. There were 39 cases of placenta previa in the series. All were diagnosed correctly, except for 3, in which marginal placenta previa was present. No maternal mortality and no increased neonatal or fetal mortality resulted from these "false negative" diagnostic errors. No incorrect diagnoses were made when cystography was done.

The author has had difficulty in visualizing the placenta in cases of twins, marked hydramnios, and in normal pregnancies of a duration of less than 28 weeks.

THE EFFECT OF VERATRUM VIRIDE ON THE URINE VOLUME, BLOOD PRESSURE AND PULSE RATE IN NORMAL AND TOXEMIC PREGNANCY

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Am. J. Obst. & Gynec., 58: 90, 1949

Veratrum viride has received new popularity in the treatment of eclampsia from the work done in recent years in Cincinnati and Boston. In 1946, Willson used veratrum viride in a series of toxemic pregnancies and found a reduction in the urinary output. He postulated that the existing hypertension was actually beneficial for the maintenance of normal kidney function. This is at variance with the views of numerous authors who have thought that the predominant element in toxemia is vasospasm.

The authors studied 10 toxemic, 3 hypertensive, and 4 normally pregnant women. All the patients were kept on bed rest and 0.9 gm. sodium chloride diet. An indwelling catheter was placed in the bladder. After a control period varying from 8 to 48 hours, during which patients received measured amounts of water, subcutaneous doses of veratrum viride were given every 2 hours from 12 to 48 hours. Following the latter period, a combined period was observed in which magnesium sulfate and 5% glucose were added to the veratrum viride.

All 4 normal patients showed no change in the urine volume, blood pressure, or pulse rate following either veratrum viride alone or combined treatment. In the remainder of the patients, a decrease in the hourly urinary output was observed, coinciding with the maximal fall in blood pressure. However, with the return of the blood pressure to a desirable level (which was always lower than the control level), the urine volume increased and was maintained even though veratrum therapy was continued. Because of this compensatory polyuria, the total urinary output for the control and veratrum viride periods maintained almost similar proportions. The combined regimen invariably showed increased

urine volume. Patients studied in the postpartum period had a marked diuresis in both the control and the veratrum viride periods.

The urea clearance test was performed on 6 pre-eclamptic and 2 hypertensive patients. The variations in this test during the various periods were considered to be within the range of error of the procedure.

In both pre-eclamptic and hypertensive groups, the blood pressure and pulse were markedly decreased following the use of veratrum viride. In general, the patients with essential hypertension required larger doses of veratrum to produce a satisfactory blood pressure fall.

This study includes 2 patients with convulsive eclampsia who were treated with veratrum viride with highly successful results. The urinary output was maintained at an adequate volume; the urea clearance was maintained at a satisfactory level.

Pharmacologically veratrum viride has 2 actions: first, it has a definite vaso-depressor and cardio-decelerator effect, mediated through a vagal reflex; second, the drug has a definite peripheral vasodilating action independent of the vagus nerve. Willson has observed a dangerous decrease in the urinary output following the administration of this drug in toxemia. A similar decrease has been observed by the authors; in no instance did this decrease reach dangerous levels of oliguria; harmful effects or symptoms of shock were not observed in any patient, despite the marked fall in blood pressure and pulse. The decrease in urine volume is more marked in the face of a sudden fall in blood pressure, severe vomiting and profuse diaphoresis, and an inadequate fluid intake. If the fluid balance is maintained with 5% glucose in water intravenously, alarming oliguria is not observed. The addition of magnesium sulfate to veratrum viride seems to be of real value in the treatment of toxemia.

HEART DISEASE AS A COMPLICATION OF PREGNANCY, WITH EMPHASIS ON INDICATIONS FOR RECOMMENDING THERAPEUTIC ABORTION OR AVOIDANCE OF CONCEPTION

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California Med., 70: 383, 1949

Two and one half per cent of women in the childbearing age have heart disease. Only a few of these women, however, have serious cardiac incapacities. Both congenital and rheumatic lesions are well or poorly tolerated in accordance with the mechanical handicap produced. Auricular fibrillation is not in itself a grave complication. Rheumatic activity is a grave complication; its incidence during pregnancy varies greatly in different localities. There is a greater tendency

toward heart failure in the older age groups, probably because the heart disease has been present for a longer time. The same is true of women of high parity. The duration of the heart disease (rheumatic) as well as the relation of the age of the patient to the severity of the heart disease, are important factors. Heart failure in a previous pregnancy is a strong reason to expect recurrence of failure in a succeeding pregnancy. There is an appreciable risk in pregnancy for a woman who is a Class III or IV cardiac. However, the overall percentages favor successful outcome.

Hypertension, *per se*, probably does not have a deleterious effect upon pregnancy. Hypertensive patients are 7 times more likely to develop toxemia than the normal patient; a previous history of toxemia in association with hypertension would be a relative contraindication to pregnancy.

Circulatory efficiency may or may not be reduced following pregnancy in a cardiac patient. The exact evaluation of this factor is difficult, and there is unquestionably a strong psychic element. In general, patients at the University of California Hospital had an increased incidence of diminution of circulatory efficiency following pregnancy as they grew older.

The cardiac load begins increasing about the 5th lunar month and this increase continues until midway of the 9th lunar month, when the load diminishes about 10% from the peak. Cohen and Thompson observed that the incidence of heart failure increases through the 8th lunar month of pregnancy and then diminishes to term. These findings have not been confirmed by Mendelson or Bunin and Rubricius. The latter authors found the onset of failure equally distributed from the 5th to the 10th lunar months.

Diminution in the vital capacity, increased venous pressure, increase of the circulation time, are all clinical signs of impending heart failure. Observation of these factors, as well as the blood pressure, the arterio-venous oxygen difference and the blood volume, is of value in determining the onset of cardiac decompensation.

The determination of type of delivery in cardiac patients has been much discussed. Numerous authors have reported an increased postpartum mortality rate in patients delivered by cesarean section. On the other hand, Sampson *et al.* found that although the physical work of labor may be negligible, if a complication develops, there may be abrupt and considerable loads of work undertaken. The author feels that occasionally a history of previous precipitation of heart failure by labor would indicate cesarean section to avoid decompensation in a subsequent pregnancy. The changes in the circulation following delivery resemble those which occur when an arterio-venous shunt is obliterated. Abrupt delivery of blood from the uterus, as with cesarean section, may be less well tolerated than the slower emptying by the repeated contractions of labor.

For patients with heart failure during the immediate postpartum period, the author recommends the following: (1) restriction of oxytocic drugs, because they precipitate an abrupt rise in venous pressure, (2) the use of mercurial diuretics, (3) venisection, unless the patient be anemic, and (4) an extended period of postpartum rest.

(This concise review of the essential facts about heart disease in pregnancy emphasizes the more important points concerning prognosis and treatment and would be acceptable, I imagine, to most obstetricians and cardiologists. As Sampson points out, either a history of previous failure or advanced age (over 35) is a most unfavorable omen; and, in my opinion, if therapeutic abortion is ever indicated, it is warranted in patients with rheumatic heart disease who have a clear-cut history of past heart failure. The old idea that cesarean section is frequently indicated in heart disease is a hard one to dispel; and many internists, I find, continue to recommend it. Although Sampson is opposed to abdominal delivery in general for this complication, he does make an exception of patients who have previously been thrown into failure by labor. My reaction to this would be that if labor will possibly produce failure in such a patient, cesarean section is still more likely to do so.—Ed.)

TUBERCULOSE E GRAVIDEZ (TUBERCULOSIS AND PREGNANCY)

CERRUTI FRANCISCO

Medicina Cirurgia Farmacia (Rio de Janeiro) 150: 583-598, Oct. 1948

CONCLUSIONS

1. Pregnancy has little influence on the evolution of tuberculosis, especially on tuberculosis under treatment.
2. Interruption of pregnancy does not improve the evolution of the bacillary process.
3. Pregnancy should not be interrupted but intensive modern phthisiotherapy should be used, as pregnancy does not restrict the full action of collapse therapy, and eventually the use of streptomycin.
4. There is no advantage in interrupting pregnancy in the advanced forms of tuberculosis.
5. In cases of initial evolutive forms which, after intensive collapse therapy in the first three months of pregnancy, have not shown improvement, abortion is indicated. Such are rare clinical occurrences.
6. Never perform an abortion after the third month of pregnancy.
7. For all practical purposes congenital tuberculosis does not exist, nor hereditary dystrophies, nor hereditary predispositions; so the child of a tuberculous woman, as a biological and social entity, is equal to the child of a healthy mother, if it is immediately isolated from exposure.
8. Premature delivery is more common than abortion in a woman with tuberculosis.
9. Hyperemesis and toxemia are rare in the pregnant woman with tuberculosis.
10. Delivery in a tuberculous woman is more rapid and less painful.
11. The delivery should be attended in a manner which is easy, short, non-exhaustive, and non-traumatic.
12. The delivery should be spontaneous when easy; if there is dystocia, it is preferable to shorten labor within obstetrical possibilities without waiting as long as in the case of a healthy pregnant woman.

13. The tuberculous patient has a tendency to postpartum hemorrhage.
14. The tuberculous woman is very prone to hemorrhages; she must be attended immediately at the first sign of shock.
15. Mortality is relatively high during the postpartum period.
16. All tuberculous patients should be submitted to lung collapse the first postpartum day and followed carefully during this period.
17. As a rule, a tuberculous woman should not nurse her baby.
18. B.C.G. vaccine should be given to the newborn.
19. It is advisable that those who have had small lesions of the productive type should become pregnant only one or two years after clinical cure; and those who have shown the exudative forms should observe a period of three or four years.
20. Precarious, social and economic conditions of patients frequently prevent the doctor from wholly resorting to the modern orientation of care of tuberculous pregnant women.

(The incidence of pulmonary tuberculosis in Latin America is high and the conclusions reached in this paper are based upon an extensive experience. The first seven conclusions as well as the last one are sound and since they deal with the practical management of the tuberculous grávida, they are the most important. Concerning some of the remaining observations I am not sure, but they merit consideration. In any event, it is good to have this expression of opinion from Rio de Janeiro.—Ed.)

A COMPARATIVE STUDY OF ACUTE AND CHRONIC APPENDICITIS IN PREGNANCY

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West J. Surg., 57: 150, 1949

The authors report 54 cases of appendicitis in pregnancy operated upon at Grace Hospital between 1943 and 1947. Thirty-one of the cases were chronic appendicitis, and 23 were acute. During a similar period, there were 21,682 deliveries, giving an incidence of 0.249% for all types of appendicitis in pregnancy.

In the chronic group, 25.8% of the patients gave a "typical" history of appendicitis. Only 45.3% of the chronic cases had no fever; the remaining patients had low grade temperatures.

General and spinal anesthetics were used, general anesthesia being used 5 times as frequently as spinal. Anesthesia apparently plays no part in initiating abortion or premature labor.

The authors believe that the McBurney incision or the Davis incision is the incision of choice during the last 6 months of pregnancy.

In the acute appendicitis series, 63.6% were either retrocecal or fixed by ad-

hesions. This was true in only 22.6% of the chronic group. In many of the fixed appendices, the surgeon recorded that their removal was difficult. Three out of four abortions occurring within the first 3 postoperative days were in this group.

In the acute group, the fetal loss was 17.4%. When the disease process was limited to the appendix, the immediate fetal loss was 7.2%, but increased to 33.3% when peritonitis was present. The fetal loss in these 2 acute groups is 2 times and 10 times greater, respectively, than in the chronic group. The high incidence of fetal loss in the acute series is due to the high incidence of spontaneous abortion and premature labor. Patients who went to full term had no fetal deaths.

In cases in which the acute process was limited to the appendix, as in the chronic cases, the incidence of spontaneous abortion and premature labor during the period of hospitalization is about the same; i.e. 7.2% and 6.7% respectively. Fetal loss in acute appendicitis with peritonitis is 5 times greater. The incidence of fetal loss increases as pregnancy advances: first trimester 4.0%, 2nd trimester 6.7%; 3rd trimester 33.3%. Symptoms of threatened abortion occurred in 3 (16.7%) of the 18 patients in the acute series and 4 (14.3%) of the 28 patients of the chronic series, who were discharged undelivered. Of the undelivered patients in the acute series, 27.8% terminated their pregnancies before full term while in the chronic series, all 24 patients went to full term after discharge.

Intraperitoneal sulfonamides, penicillin parenterally, progesterone, intravenous fluids, sedatives, intestinal intubation, and oxygen were all used. The liberal use of sedatives during the first 2 to 3 days is perhaps the best treatment, because it is during this period that spontaneous abortion and premature labor occur. The authors used progesterone in some of their cases, but in entirely too small a dosage.

The authors believe that in acute appendicitis in pregnancy, appendectomy is the procedure of choice. Cesarean section prior to the appendectomy is a violation of all obstetrical and surgical principles.

SICKLE CELL ANEMIA AND PREGNANCY

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Am. J. Obst. & Gynec., 58: 75, 1949

In the previous literature, 33 cases of sickle cell anemia in pregnancy have been reported; 7 maternal deaths occurred in this group. The present series deals with 11 cases of sickle cell anemia in pregnant women seen at the Johns Hopkins Hospital from 1927 to 1947, with no maternal deaths.

Sickle cell anemia was diagnosed by marked anemia, evidence of red blood cell regeneration, elevated icteric index, and marked sickling of the red blood cells. In addition, leg ulcers, abdominal and joint pains, and asthenic habitus

were useful in leading to the diagnosis. All patients were diagnosed during the prenatal period, and all were admitted to the hospital for treatment and study prior to delivery. In some cases, the anemia was extreme, the hemoglobin being less than 40%.

The average amount of blood given to each patient was 2,650 cc. during the period of gestation and immediate puerperium. Among 52 transfusions, 12 transfusion reactions occurred. Eleven of these were simple febrile reactions; one was of a severe type, accompanied by abdominal pain and hemoglobinuria. Febrile conditions usually related to infections, including pyelitis, meningitis, episiotomy infection, and brain abscess, were commonly encountered. Hemolytic crises occurred in only one case in pregnancy and in 3 cases during the postpartum period. One patient had a cerebral thrombosis. Three women had mild to severe toxemia. Complications during labor and delivery were minimal. Study of the placenta showed no abnormality of fetal-placental weight ratio. Sickling of the maternal blood cells in the placenta was demonstrable in 2 cases, but sickling of the fetal blood could not be shown. Five infants were studied for sickling, with no positive results.

Among the 11 mothers, there were 17 pregnancies. Thirteen of the infants weighed 1,000 grams or more. Three of these infants died: one following induction of labor because of cerebral thrombosis in the mother; the second, following severe pre-eclampsia; the third (and only full-term death) followed a forceps rotation. All of the patients were alive at the time of the writing of this paper except one. This woman died 2 years postpartum of chronic glomerulonephritis.

Various authors maintain that the sickle cell anemia patient is slender and underweight with an increased dorsal kyphosis and lumbar lordosis. In 3 of the 5 pelvis measured by clinical pelvimetry in this series, outlet contraction was found to be present. In 2 other cases, the diagonal conjugate was less than 11.5 cm. X-ray pelvimetry was obtained on 4 patients. Three of the 4 had convergent side walls with heavy blunted ischial spines. The sacra were straight with no forward rotation. The pelvis had a tendency to be anthropoid.

The largest number of deaths in sickle cell anemia are those associated with intercurrent infection and vascular disease. In pregnancy, constant medical observation and frequent hospitalization for investigation and treatment of toxemias and febrile states are mandatory. Liberal use of chemotherapy and blood transfusion is required. Transfusion is particularly indicated for the purpose of maintaining the exchange of oxygen between mother and fetus. It is advisable to use sodium lactate solutions along with transfusions not only to prevent renal complications, but possibly to reduce the sickling tendency by raising the pH of the blood. Anesthesia for delivery is an individual matter. However, block anesthesia offers some advantage over inhalation anesthetics, particularly with regard to the fetus.

The question of therapeutic abortion and sterilization in this disease has been studied. Although simple sickle cell anemia is inherited, there is no way to predict which cases will develop sickle cell anemia. As yet, the prognosis of children born to mothers with active sickle cell anemia cannot be stated with assurance. Therefore, therapeutic abortion for sickle cell anemia alone would not be justified.

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PATHOLOGY OF LABOR AND PUERPERIUM

THE ROLE OF MASSIVE BLOOD TRANSFUSIONS IN THE MANAGEMENT OF RUPTURED UTERUS AND OTHER SERIOUS OBSTETRIC SHOCK

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South. M. J., 42: 263, 1949

Infection, so long the preponderant cause of obstetric deaths, now shares its position with hemorrhage as the principal cause of maternal mortality. At the present time, hemorrhage and shock are undoubtedly the most important causes of maternal fatalities.

The science of modern blood transfusion had its inception in obstetrics in 1818, at which time James Blundell gave an infusion of blood to a woman following postpartum hemorrhage. Approximately a century later, obstetricians began to make practical use of this discovery and whole blood transfusions have been used freely since that time.

Citrated whole blood properly matched for Rh and A and B substances should be available. Large amounts of blood are safely and quickly given with the aid of a closed transfusion bottle with drip attachment. Repeated observations showed that 100 cc. of blood can be given per minute through a single transfusion unit when an 18 gauge needle is used.

Six cases are reported in which massive hemorrhage was the major problem; four of these patients had rupture of the uterus. No patient received less than 3500 cc. of blood. One patient received 7500 cc. of blood.

No institution is equipped for obstetrical care unless it has a good blood bank. There is no place in obstetrical shock for saline, dextrose or plasma. Speed is an absolute essential. Any patient who is a candidate for shock should have an 18-gauge needle in a vein and fluids running so that she can be immediately transfused if the occasion arises. The amount of blood required is that which will restore the normal efficiency of the circulation as measured by the pulse, respiration and blood pressure. The hemoglobin and hematocrit determinations must be normal before treatment can be considered adequate. Oxygen, antibiotics, anesthesia, and gastro-intestinal decompression are indispensable accessories to massive transfusions.

(Largely as the result of transfusion experience during the war, the administration of massive amounts of blood rapidly became established as both a feasible and a lifesaving measure; and today it is not uncommon for exsanguinated patients to receive as much as 6,000 cc. within a relatively short period. In certain cases of abdominal pregnancy, in rupture of the uterus and in other dire hemorrhagic complications in obstetrics, such

Sterilization will rarely be necessary, since patients with sickle cell anemia have an average of only 2 pregnancies. Moreover, 20% of these pregnancies terminate in abortion.

PREGNANCY IN ADDISON'S DISEASE

Report of Four Patients

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J. Clin. Endocrinol., 9: 514, 1949

The presence of the adrenal glands is not essential for the establishment or maintenance of pregnancy. There are available 29 reports covering 39 pregnancies in women with Addison's disease, 30 of whom continued to term. In one such patient, studies of the steroid excretion showed values corresponding to the amount excreted in normal pregnancy. There is usually a deterioration of general health in women with Addison's disease complicating pregnancy.

This report covers 4 patients with proved Addison's disease who were studied during 5 pregnancies. One pregnancy ended in spontaneous abortion, a second was terminated by D & C., and a third by hysterectomy. Two patients went to term: one was delivered by section, and the other spontaneously.

In all these patients, the urinary excretion of gonadotropin was normal. The values obtained for sodium pregnandiol glucuronidate and estrogens, though low, were within the range seen in normal pregnancies. Corticoid activity could not be demonstrated in the urine of one patient studied in the third trimester. The urinary excretion of 17-ketosteroids was increased late in pregnancy in the 2 patients in whom gestation carried to term.

The nausea and vomiting in the first trimester of pregnancy is best managed by electrolyte replacement with saline infusions. In the last trimester, the increased blood volume and the possible contribution of hormones from the fetal adrenals might have a theoretical favorable effect upon the adrenal insufficiency.

However, serious difficulties might be anticipated at the time of delivery as a result of blood loss, and again in the postpartum period during the diuresis which commonly occurs at that time. The authors' patients were carried upon a maintenance dosage of desoxycorticosterone acetate (DCA) as well as electrolyte replacement and intravenous fluids as indicated. At the termination of each pregnancy, therapy consisted of the administration of DCA by injection and sodium chloride by mouth; and parenteral saline, glucose, plasma, and whole blood as indicated. Each patient also received whole adrenal extract (ACE).

Following delivery, increased manifestations of adrenal insufficiency occurred in one case; the other had a benign postpartum course.

In 3 cases, hydrocephalus was not recognized and caused obstructive dystocia followed by spontaneous rupture of the uterus and death. In 4 cases death was due to rupture of an upper uterine segment scar; 3 had had cesarean sections, and one a myomectomy. In 8 cases, spontaneous rupture of the uterus was due to varied and unknown causes. In this last group, dense cervical scarring played a conspicuous role.

Among the traumatic ruptures of the uterus, 20 cases were the result of version. Versions were done for the following causes: 8 for transverse presentation, 6 for placenta previa, 5 following failed forceps, and one for ovarian tumor. The authors feel that in the treatment of placenta previa, all forms of version should be abandoned. Other causes of traumatic rupture included: difficult forceps operations (9 cases), craniotomy (3 cases), strong fundic pressure (3 cases), Pinard maneuver (1 case), and bagging (1 case).

Diagnosis of uterine rupture during labor is often missed, partly because uterine rupture is rare in the experience of any one obstetrician and partly because the obstetrician fears that he may open the abdomen by mistake. Procrastination is the most common cause of death in rupture of the uterus.

In abnormal fetal attitudes or when there is an obstacle to delivery, if the cervix is fully dilated and the vertex remains unengaged, the lower uterine segment is greatly stretched and rupture of the uterus is threatened. At that time, sudden and complete relief of the pain of labor with cessation of the contractions is evidence of rupture. The presenting part may recede; the fetus may escape from the uterus; and the fetus may die at once. On the other hand, if the fetus is fixed deep in the birth canal, it may not escape from the uterus, and may be delivered alive. When rupture of the uterus is the result of internal version, the diagnosis is most often missed; this is because it is assumed that the hemorrhage and shock are due to trauma and anesthesia and not to rupture. Any major vaginal operative procedure in obstetrics should be followed by exploration of the uterus. The danger incident to examination of the uterine cavity is far less than the risk of delay or failure of diagnosis.

Tetanic uterine contractions may be controlled by ether or chloroform. Operative procedures must be done with the utmost gentleness in the face of impending rupture. Internal version is absolutely contra-indicated. If slight trial traction on forceps fails to deliver the head, perforation of the head or cesarean hysterectomy may be necessary.

The cardinal principles of good treatment are massive transfusion and immediate operation. Rupture of an old cesarean section scar may sometimes be handled by resuture. If hysterectomy is done, it should be rapid. If necessary, the operation may consist only of rapid excision of the uterus between broad ligament clamps and abdominal closure with through-and-through sutures; the clamps may be removed on the 3rd day. If rupture of the lower uterine segment is minimal and known to be incomplete and hemorrhage into the broad ligament and parametrium is not great, the rupture may be repaired from below. If there is any doubt about complete control of hemorrhage, the abdomen should be opened at once. Tamponade may at times be satisfactory, but it is not advised.

transfusions spell the difference between life and death; and certainly in the two conditions mentioned, preparations should always be made for giving blood in large quantities.

The mention of James Blundell in the above article calls to mind the fact that history has treated him rather shabbily for his contributions were actually greater than those of many better known men. Among them may be mentioned: (1) At a time when blood transfusion was actually forbidden by law in Paris, so fatal had it proved, Blundell carried out careful research on the problem, stated that lower animal blood should never be used for transfusion in humans (as had previously been customary) and himself performed six transfusions between 1820 and 1825, followed by at least four more that date to 1852. His first successful transfusion was in 1825 on a woman who was dying from hemorrhage in childbirth. Students of the history of blood transfusion regard him as the great pioneer in this field. (2) In connection with cesarean section, from which operation only a single recovery was on record in the United Kingdom in 1824, Blundell proposed the extirpation of the uterus after the operation with the object of reducing the appalling mortality. This suggestion was founded on the results of numerous experiments on the uteri of pregnant rabbits in the course of which he lost all by cesarean section but saved three out of four in which he ligatured and amputated the uterus. Fifty years later this operation was introduced by Porro of Pavia and has since, of course, been known by his name. (3) Blundell was the first surgeon in Great Britain to attempt to cure cancer of the uterus by hysterectomy per vaginam. On February 19, 1828, he performed such an operation with satisfactory operative recovery but a year later the patient died with distention of the abdomen associated with obstinate constipation. This is sometimes referred to as the first successful hysterectomy for cancer in Great Britain and is discussed in graphic fashion by A. J. McNair in *Guy's Hospital Reports*, July, 1928,—a century after the operation. (4) Blundell was on the verge of realizing the contagious nature of puerperal fever and wrote "Gossiping friends, wet nurses, monthly nurses, and the practitioner himself are the channels by which, I suspect, the infection is principally conveyed."—Ed.)

DIAGNOSIS AND MANAGEMENT OF RUPTURE OF THE UTERUS WITH A STUDY OF 64 MATERNAL DEATHS

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Am. J. Obst. & Gynec., 58: 117, 1949

This report covers 64 maternal deaths from rupture of the uterus occurring in Brooklyn between January 1937 and January 1948. In 48 cases, the site of rupture was recorded. Rupture occurred in the upper segment in only 3 cases. In the remainder it took place entirely or principally in the lower segment, chiefly laterally. The patients included 7 primiparas and 57 multiparas. On the basis of etiology, 27 cases were classified as spontaneous and 37 as traumatic.

Among the cases of spontaneous rupture, 8 were grand multiparas. The authors believe that old cervical scarring is an important factor in spontaneous uterine rupture in this group. Four patients received posterior pituitary extract during the first stage of labor. It had also been administered to an occasional patient in the series, but in these 4 cases, appeared to be responsible for the rupture.

confinement had often been complicated: accidental hemorrhage in 4 cases, dystocia and forceps delivery in 7, and section under general anesthesia in one.

It is just as difficult to find an adequate explanation for atonic postpartum hemorrhage as it is for atonic non-detachment of the placenta. In the first instance, the uterus has functioned well and easily in the first and second stages of labor, is atonic in the third stage, but retracts excellently as soon as the placenta is out. In atonic postpartum hemorrhage, the uterus has often had difficulty in the first and second stages of labor, retracts excellently in the third stage and expels the placenta easily, but becomes atonic after the placenta is out.

RUPTURES OF THE UMBILICAL CORD WITH A CASE OF INTRA-PARTUM RUPTURE OF ALL THREE VESSELS

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California Med., 70: 422, 1949

Umbilical cord rupture may be partial or complete. Complete ruptures have been reported at least 7 times in the literature. Rupture of the cord may be the result of velamentous insertion, absolute or relative shortness, localized necrosis, trauma due to operative manipulations.

The authors report a case of a 25 year old primigravida who entered the hospital in labor one week past term. No abnormalities were noted until the cervix was fully dilated and the vertex was 2 cm. below the ischial spines. Suddenly the fetal heart became exceedingly rapid and then ceased. A forceps rotation and extraction was immediately done. A large amount of meconium and a small amount of dark red blood escaped. The umbilical cord was looped once around the infant's neck and once in a complete turn around the right antecubital fossa. In the latter area, all 3 vessels were completely severed. There was no active bleeding and no more than 5 cc. of free blood was observed. Careful inspection revealed that the tear had occurred at a natural kink in the cord. This kink showed a lesser and a greater curvature and it would seem that the continued tension on the cord late in labor caused the inner curvature to give way. The fetal death is believed to have been the result of asphyxia rather than hemorrhage.

(The data and teachings in this article speak for themselves. As mentioned in previous editorial notes, the senior author deserves great credit for his continual emphasis on the fact that hemorrhage is the number one killer of childbearing women.—Ed.)

RETAINED PLACENTA AND POSTPARTUM HAEMORRHAGE

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Brit. M. J., 1: 849, 1949

The author studied 98 patients who died with complications during the 3rd stage of labor. Sixty-six of these patients died as a direct result of hemorrhage and shock; the other 32 had hemorrhage and shock but recovered temporarily; they died later in the puerperium from other causes.

There were 73 cases of retained placenta. In the analysis, the placenta was considered "retained" if there was delay or difficulty in its delivery, and if severe hemorrhage occurred early in the 3rd stage and necessitated emergency measures for the removal of the placenta. There were 2 cases of retention due to constriction ring. Both patients had manual removal of the placenta, but died a few hours later. There were 45 cases of atonic non-detachment of the placenta, 18 cases of partial adhesion of the placenta, 6 cases of complete adhesion, and 2 cases of intraperitoneal rupture with escape of the placenta into the peritoneal cavity.

The factors to be considered as leading to death from retained placenta are blood loss, traumatic shock due to the manner of removing the placenta, and the length of the 3rd stage of labor. The patients may die from hemorrhage unless treated early by adequate blood transfusion. However, many patients have relatively little blood loss, and death seems to be due essentially to shock.

In the hospital where these necropsies were performed, there were 3 obstetric units. In one there were strict rules that there should be no interference with the uterus. The 16 early deaths in the unit where non-interference was the rule were not significantly different from the 13 and 11 deaths in the other 2 units. So far as these figures go, they suggest that, though forcible expression and manual removal may not be ideal procedures, their omission in cases of retained placenta is just as harmful to the patient as their performance.

The most striking point in the series of necropsies is that the 3rd stage of labor had been allowed to continue for 3 hours or more. Most of the deaths occurred in cases in which the placenta had been left in utero for 3 to 7 hours.

There were 25 cases of severe hemorrhage following delivery of the placenta; 16 of these died within 7 hours after delivery. There were 6 cases of ruptured uterus and 19 cases of atonic post-partum hemorrhage. In every case of atonic postpartum hemorrhage, the placenta had been delivered easily. However, the

only 200,000 units of aqueous penicillin upon admission to the delivery floor; moreover, the majority of positive cultures were obtained more than 48 hours following delivery.

The results seem to indicate that relatively high dosages of penicillin may eliminate penicillin-sensitive organisms from the uterus for at least 3 days or more postpartum. The fact that penicillin therapy will usually disinfect the postpartum uterus has very extensive clinical applications.

PENICILLIN THERAPY IN THE OBSTETRICAL PATIENT

A Study of Its Effect on the Bacterial Flora of the Postpartum Uterus

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Am. J. Obst. & Gynec., 58: 101, 1949

It is known that the gravid uterus is ordinarily sterile before the 6th hour of labor, but is usually not sterile after that time. The postpartum uterus almost always contains numerous bacteria. Cultures were obtained from the uterine cavities of 86 postpartum patients, 54 of whom received penicillin, and 32 of whom were not treated. The material was inoculated into Brewer's thioglycollate medium. Clarase and ascitic fluid were added to the medium. The organisms isolated were of the species generally accepted as representing the normal flora of the postpartum uterus; in addition, pleuropneumonia-like organisms were isolated from the uterus for the first time during this study. They did not appear to be pathogenic.

Patients in the control series received no penicillin prior to culture. They were selected on the basis of a normal temperature and the cultures were obtained 36 to 72 hours after delivery. Thirty of the cases showed various bacteria, predominantly anaerobic streptococci and bacteroides. These organisms were found to be highly sensitive to penicillin in vitro. The remaining 2 cultures were sterile.

The patients who received penicillin were cultured at random, since the patients were placed on penicillin as soon as they reached the delivery floor. The amount of penicillin given was intentionally varied in order to determine the smallest dosage necessary to sterilize the uterine cavity. The largest dose given was 400,000 units daily, in doses of 50,000 units every 3 hours. The smallest dose was a single intramuscular injection of 200,000 units which was given as soon as the patient was admitted to the delivery floor. The period elapsing between delivery and culture was also deliberately varied, in order to determine how long the uterine cavity would remain sterile. The majority of cultures were obtained within 36 to 72 hours postpartum.

Among the 54 patients who received penicillin, 32 had sterile cultures, aerobically and anaerobically, regardless of the penicillin dosage or the time of culture. Eight further cases showed only pleuropneumonia-like organisms. The remaining 14 included 8 who showed anaerobic streptococci; the remainder had gram-negative rods, *Gaffkya* and the anaerobic and aerobic diptheroids.

A comparison of the 2 series shows that 6.2% of the control series had sterile cultures, whereas 59.4% of the penicillin series were sterile. The majority of positive cultures in the penicillin series were obtained from those cases receiving

although spasmodic, irregular, and shallow intrauterine respiration differs only slightly in pattern from extrauterine respiration, the major change being substitution of air for fluid. Farber and Sweet (*Am. J. Dis. Child.*, 42: 1372, 1931) believe that obstruction of placental circulation with resultant intrauterine anoxia initiates premature respiratory movements in utero with aspiration of amniotic contents.

In the present series, varying amounts of amniotic contents were found in the lungs of infants known to have experienced intrauterine anoxia or hypoxia from such causes as abruptio, prolapse of the cord, and erythroblastosis. A vernix membrane was not demonstrated in any of these infants. Therefore, although intrauterine anoxia may lead to exaggerated respiratory movements, this should not be considered the dominant factor responsible for the vernix membrane. Many newborn infants have been subject to varying degrees of intrauterine anoxia and a membrane can be demonstrated in only a few.

The sebaceous glands of certain fetuses are, no doubt, more active than those of others. The amount of amniotic debris and vernix varies between individuals. In addition, vernix may be concentrated not only in the amniotic sac but also in the respiratory passages. Theoretically, in the presence of large amounts of concentrated vernix, extremely high in lipids, conditions are right for development of vernix membrane.

An attempt was made to produce a membrane in the alveoli of several lungs removed at autopsy from stillborn infants. Centrifuged amniotic fluid sediment was injected into a heated lung. The latter was subjected to alternating negative and positive pressure. A membrane was not formed. However, the authors feel that the fluid injected was not sufficiently high in lipids to produce the characteristic picture.

The authors observed a high incidence of pneumonia in association with the vernix membrane. Perhaps the presence of pneumonia causes abnormal stickiness of the cells lining the respiratory passages, such as occurs in endothelium during the phenomenon of inflammation, thereby permitting greater adhesive surfaces upon which vernix may be deposited.

Following cesarean section, if adequate immediate aspiration is done, the mortality rate may be lowered from 2 to 10%. This lowering of death rate is, according to the authors, chiefly in a "pseudo-membrane" group of cases. This suggests that immediate intra-tracheal aspiration may in some cases prevent aspiration of excessive amounts of amniotic debris and more extensive membrane involvement. In the experience of the authors, active resuscitation with the Torpin insufflator has not significantly increased the occurrence of the membrane.

The authors conclude that the vernix membrane prevents exchange of gases in opened alveoli. The membrane is extremely high in lipids and is present in large amount in the respiratory tract before birth. The necessary factor concerned with development of the membrane is concentration of vernix which has an extremely high lipid content. Pneumonia prepares a fertile field for such development. Exaggeration of intrauterine respiratory movements is a factor only in those cases presenting the aforementioned prerequisites. Aspiration may

THE NEWBORN

ASPHYXIA NEONATORUM AND THE VERNIX MEMBRANE

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Arch. Path., 47: 307, 1949

A significant number of asphyxial neonatal deaths are believed to be caused by vernix caseosa plugging the bronchioles and lining the alveolar ducts and walls. In a study of pneumonia, Johnson and Meyer (*Am. J. Obst. & Gynec.*, 9: 151, 1925) encountered several newborn infants with a hyaline membrane coating the walls of the smaller respiratory passages. They believed that it was derived from dissolution of the epidermal cells and fat of vernix caseosa, which was converted into a viscous layer. The membrane was never observed in stillborn infants; it was accordingly believed that intrauterine aspiration of amniotic fluid was a necessary antecedent. This aspiration was believed to be the result of respiration in utero following some factor producing anoxia. Vernix membrane was observed to be particularly frequent following cesarean section. It was frequently noted to occur without inflammatory reaction.

Some infants who live for a period of a few hours to 4 days, exhibit a fairly characteristic syndrome. They may breathe normally or be slow to breathe at birth, but eventually there develops an increasing struggle for breath. At autopsy, these lungs sink when placed in water. Microscopically, an eosinophilic hyaline membrane is seen, plastered against the walls of alveoli, alveolar ducts, and respiratory bronchioles. This membrane readily stains for fat. Vernix caseosa of exceptionally high lipid content and containing many epidermal cells is seen plugging the terminal bronchioles where these join the alveolar ducts. The alveolar ducts and alveoli which are lined with the membrane remain open. Most of the remainder of the lung is collapsed.

The authors studied 119 consecutive autopsies on infants dying between 1938 and 1947. Routine sections of the lungs were made with H & E. If vernix membrane was suspected to be present, Sudan IV was also used. The authors report 6 cases in detail. All these infants were born at full term. Two of the labors were normal, one was precipitate, one was not fully documented, and 2 infants were delivered following an inertia type of labor. In one of the latter, labor was stimulated with pituitary extract. The infants lived from 18 hours to 6 days. At autopsy, all of the lungs showed vernix membrane, and 4 showed inflammation of the lungs as well. The total number of infants with vernix membrane was 7 or 5.8% of the total number of cases on whom necropsies were performed.

The studies of Davis and Potter (*J. A. M. A.*, 131: 1194, 1946) indicate that spasmodic and irregular respiratory movements occur even in early fetal life,

of more than 65,000 pairs of dizygotic twins (U. S. Vital Statistics reports, 1941, 1942, and 1945) revealed in each year's group approximately 27% more like-sexed than unlike-sexed pairs. This preponderance of the like-sexed over the unlike-sexed pairs in the dizygotic group is beyond the possibility of chance. Greulich, in 1934, reported 538 sets of twins. There was a total of 171 unlike-sexed to 271 like-sexed twins, after the definitely monozygotic group had been eliminated. This is a ratio of 134.5 per 100.

Experiments were undertaken with rats of the Osborne-Mendell strain. It was felt that the easiest approach to the problem was to produce pregnancies by inseminations through normal mating, permitted only at definite times in the latter part of the heat period. This was assumed to be the latter part of the fertility period. The total output of the medical school rat breeding colony for the year 1945 was taken as control. In this group, of 12,135 offspring reaching the age of 21 days, there were 6,071 males and 6,064 females in a total of 1,540 litters, or a ratio of 100.1 males per 100 females. In 1947, in 10 experiments carried out in the delayed insemination group of rats, there were 458 offspring with a ratio of 149 males per 100 females. This gave a 49% increase in the percentage of males over the control group.

In 1948, many of the unsatisfactory physical conditions in the laboratory were remedied. In addition to the control figures taken from the medical school breeding colony, an additional control group was run, using the same groups of animals under identical conditions as in the late insemination experiments, except for the fact that the males and females were together continuously. Each group of rats used once for a control experiment, was used both before and after this time for late insemination experiments. In 6 control groups, there were 480 offspring. The ratio of males per 100 females varied from 74 to 107, an average of 91. In the breeding colony control group and in the controls in the experimental colony, from 40-60% of the litters were approximately evenly divided, from 20-30% of the litters showed 60% or more females and another 20-30% showed 60% or more males. In the late insemination experiments there was no litter with as many as 60% females, only 4 litters were relatively equally divided, while the great preponderance of litters (27) showed from 60-100% males.

These experiments are based on the knowledge that the great majority of rats go into heat within a period of a relatively few hours, and that for most rats ovulation follows within 7 to 10 hours. The resultant deviation of the sex ratio from the average, with the high percentage of males in practically all litters, brought about by simply postponing mating from the presumed normal time, is very obvious. It is the opinion of the authors that in most animals there is a broad band in the heat period during which mating most frequently occurs, with a resulting relatively equal sex ratio. As an evolutionary process, the maximal mating response would come to lie in the period resulting in the sex ratio optimum for the propagation of the species. Theoretically, with the passage of time during the fertility period, there might be a change in: (1) the permeability of the ovum; (2) the viability and aggressiveness of the extrachromosome spermatozoa; (3) the motility of the extrachromosome spermatozoa as compared

be useless if most of the vernix is beyond the tracheal bifurcation. In other cases, however, it may forestall more extensive involvement of the lung and subsequent exitus.

(The significance of the vernix membrane continues to be an enigma, especially if the doctrine of intrauterine respiration as a normal phenomenon be accepted. Thus, if the amniotic fluid is continually being aspirated into the pulmonary alveoli by the fetus in utero, it is difficult to understand why some degree of vernix membrane is not encountered more frequently than it is. The authors endeavor to explain the discrepancy on the grounds that a quantitative factor is at work, exaggerated respiratory movements and a large amount of vernix being prerequisite to the formation of the membrane. This may be the correct solution of the problem but it does not seem to me altogether satisfying; and more work on the vernix membrane will be necessary before its nature and significance can be definitely established.

We have not been in the habit of carrying out routine intratracheal aspiration on cesarean section babies on the grounds that the trauma occasionally produced may offset the benefits achieved. This, however, is another moot question with much to be said on both sides.—Ed.)

SEX RATIO: EXPERIMENTAL STUDIES DEMONSTRATING CONTROLLED VARIATIONS—PRELIMINARY REPORT

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Ann. Surg., 129: 550, 1949

Theories as to the factors responsible for intra-uterine sex differentiation have been varied. It has been observed clinically that when insemination occurs early in the fertility period, the resultant offspring is more likely to be female, and when insemination occurs late in the fertility period, the resultant offspring is more likely to be male. In the middle of the fertility period, the sex ratio is presumed to be approximately equal. In rabbits, there is a marked shift in the sex ratio, giving a preponderance of males as the time of insemination approaches the time of ovulation. Experimental results on delayed insemination in the rat further substantiate this concept. Seymour and Koerner in 1941 studied 9,489 births resulting from artificial insemination; there was a preponderance of males (5,676 males to 3,813 females). The series showed a 48% increase in the males over the theoretically expected number. This increase might be attributed to the fact that artificial insemination was probably carried out at, or following ovulation in a larger percentage of cases than would occur in the normal course of sexual relationship.

If the concept that early insemination results in a preponderance of females and late insemination results in a preponderance of males, is correct, there would necessarily be a preponderance of like-sexed dizygotic twins. An analysis

The rhythm of breathing was irregular and was classified from the most immature type to a supernormal type: type 1, Cheyne-Stokes with irregularity; type 2, Cheyne-Stokes with apnea; type 3, rhythmic breathing without apnea; type 4, regular normal; and type 5, supernormal, stimulated. All 10 infants showed some degree of irregularity when breathing air, from a slight occasional short breath to Cheyne-Stokes breathing with irregularity. The rhythm of breathing in the low oxygen mixture was of Cheyne-Stokes periodicity, with gross irregularity in 6 infants. Four infants changed from a normal rhythm in air to a Cheyne-Stokes rhythm in low oxygen. The rhythm in all infants in the 70% oxygen atmosphere changed to or remained a regular, steady, normal type 4. The high oxygen atmosphere abolished any tendency to Cheyne-Stokes breathing. The rhythm under carbon dioxide stimulation was steady, rapid and increasing in rate or depth until the infant awoke, constituting type 5, or supernormal breathing.

The average minute volumes were 731.3 cc. in air; 792.3 cc. in the low oxygen mixture; 993.9 cc. in the high oxygen mixture, and 1,660 cc. in the mixture of carbon dioxide and oxygen.

The average tidal air volume was 16.5 cc. in air; 18.7 cc. in low oxygen; 20.7 cc. in high oxygen, and 33 cc. in an atmosphere of carbon dioxide and oxygen. The infants breathed an average of 113.5 cc. per pound per minute when breathing air, 124.5 cc. per pound per minute when breathing 12% oxygen; 153.2 cc. per pound per minute when breathing 70% oxygen; and 259.7 cc. per pound per minute when breathing 5% carbon dioxide in oxygen.

Regardless of the cause or physiologic significance of Cheyne-Stokes breathing, it is seen in connection with serious conditions. The administration of a high oxygen mixture seems to relieve the condition causing it to the point of abolishment. The authors state that oxygen is the most valuable single therapeutic agent available for a premature or full term newborn infant who is showing any sign of respiratory difficulty. It should be used early and generously.

(The observation that oxygen-carbon dioxide mixtures produce supernormal breathing in the newborn is of considerable clinical importance in the management of respiratory difficulties in premature infants. Theoretically it might seem that the hyperventilation thus produced would be beneficial in correcting atelectasis and in affording full oxygenation; actually, these possible benefits are more than offset, as a rule, by the exhaustion which this excessive respiratory activity produces and on several occasions I have gained the impression that efforts to stimulate respiration in premature infants with carbon dioxide mixtures, although momentarily dramatic, have proved to be a determining factor in the infants' death. As they state in the last paragraph of the abstract, the reaction of the authors seems to be similar.—Ed.)

with the male producing spermatozoa; and (4) genital tract conditions. The effect of the time factor on the sex of the offspring is easiest explained on the basis of the relative differences in motility, viability and aggressiveness of the 2 types of spermatozoa.

(Attempts at artificial manipulation of the sex ratio have been a favorite pursuit of many investigators. One of the most widely publicized of these was the claim in 1932 by Unterberger that an alkaline vagina yields boys and an acid vagina girls; and he maintained that if a boy is desired, a douche of one per cent sodium bicarbonate just before coitus is all that is needed to obtain the desired result. Unterberger's work was featured by the lay press and countless couples tried it out but without more than 50 per cent success.

The theory advanced by Hart and Moody in this preliminary report has been put forth in various forms back to the days of Hippocrates. Prior to the present paper, the most recent claim that the time of conception in the cycle affects the sex of the fetus was advanced by Siegel in a series of German publications. He analyzed data on the sex of the child in relation to the time of conception in 115 German women delivering during World War I. In each instance the soldier husband had only a short furlough, so that the time of conception could be accurately determined, and its position in the menstrual cycle ascertained. It would appear that Siegel's results were just the opposite from those of Hart since he found in 31 cases in which coitus took place between days 15 and 23 in the cycle that 84 per cent of the offspring were females.

Studies of this problem are subject to various sources of error. The employment of twin pregnancies in any problem dealing with sex ratios is fraught with the difficulty that the differentiation between dizygotic and monozygotic twin pregnancies is not so simple as we used to think; and modern evidence is pointing to the fact that the percentage of monozygotic twins is decidedly higher than was formerly estimated. In regard to the experimental work reported, this is quite impressive but it is based on the belief that ovulation takes place at a certain time in the day and is not documented by vaginal smear technique. Since this is a preliminary report, the authors very probably will strengthen the evidence in regard to the actual time of ovulation in their animals. Meanwhile it would be my feeling that this interesting and important work should be held sub judice.—Ed.)

IRREGULARITIES OF BREATHING IN THE NEWBORN PERIOD

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Am. J. Dis. Child., 77: 592, 1949

The rate of respiration, the irregularities of rhythm, the minute volume and the tidal air volume were studied in 10 normal newborn infants in air, 12% oxygen, 70% oxygen and 5% carbon dioxide in oxygen. The 10 babies ranged in age from 5 to 30 days. Their weights ranged from 2,381 gm. to 3,232 gm. All were healthy, newborn babies, free from infection or recognized congenital deformity. Records were taken only during sleep.

The average rates of respiration were: 46.5 per minute in air, 44.5 per minute in 12% oxygen, 53 per minute in 70% oxygen, and 51.3 per minute in the mixture of carbon dioxide and oxygen.

The uterus increases in weight from $1\frac{1}{2}$ ounces to 1.5 pounds. During this period of extensive growth, it develops great contractile power which remains dormant. In the rabbit the principal period of uterine enlargement occurs between the time of implantation and the 24th day. From this time until term (32 days) there is no further uterine growth, but merely stretching of the myometrium. Similar conditions exist in the rat, cow, monkey and man. In short, there comes a time when the fetus is too large for its environment.

During the period of uterine enlargement, the conceptus is spheroidal. During the period of uterine stretching, the shape has changed: it is now elongated and cylindrical. In the rabbit, conversion from spheroid to cylinder occurs within the space of a few hours. The uterus is subjected to increasing tension until a critical condition develops. Then suddenly the conceptus changes into a cylinder in shape, and the tension is relieved. The tension required to distend a cylinder is directly proportional to the radius; in a sphere, it is proportional to the square of the radius. Therefore, during the period of rapid fetal growth and uterine stretching, the tension is reduced to a minimum.

The earlier the time of conversion in gestation, the longer is the period of relatively little uterine growth. Thus the duration of the period of uterine stretching depends upon and is proportional to the period of rapid growth of the fetus.

Following the previous conclusion, it may be postulated that fetal maturity at birth is proportional to the total duration of pregnancy which the fetus spends in an elongated uterus. This concept is partially supported by incomplete evidence on the hamster, rat, rabbit, and guinea pig. These data relate to ossification, tolerance of anoxia, and development of reflexes. It appears that there is an innate maternal mechanism which controls the size of the offspring at birth. This is evident by the cross breeding of large stallions with Shetland ponies. The offspring are always of the same size as the newborn Shetland pony.

Progressive increase in the size of the conceptus is associated with an attendant decrease in blood flow until the time of conversion. Then there is a sudden, intense, but transient decrease of flow of blood through the uterine vessels. Following conversion, the rate of blood flow is restored to the usual level. At this time, the welfare of the fetus may be endangered.

Conversion occurs in man between $\frac{2}{10}$ and $\frac{3}{10}$ of the way through gestation. Every week after conversion is an added guarantee of full maturity at birth. The obstetrician needs a concrete physical sign of conversion. Just prior to conversion in animals, the uterus is firm and tense; immediately afterwards it is loose and soft; later fetal growth takes up the slack again. This transient softening might be a detectable sign of conversion. Change in abdominal profile, or perhaps a change in the uterine souffle may indicate uterine conversion.

(Those of us who have followed Reynolds' contributions to the literature from time to time have learned to look forward to them because they invariably present new concepts; and the above paper is no exception to this generalization. The time in human pregnancy when conversion is believed to take place, namely, around the twenty-eighth week, is a stage when several other important alterations begin to manifest themselves. Thus, the water metabolism of the body appears to undergo a change with a resultant shift in the

OPISTHOTONUS FETALIS

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West. J. Surg., 57: 165, 1949

The author reports a case of opisthotonus fetalis, or exaggerated hyperextension of the cervicodorsal spine. The patient was a 24 year old primigravida whose L.M.P. was Dec. 29, 1946 and E.D.C. was Oct. 5, 1947. Her pelvic measurements were normal and her prenatal course was uncomplicated. Examination on July 1, 1947 revealed the fetus to be presenting in left sacrotransverse position. On Sept. 22, 1947, abdominal palpation suggested a transverse lie. X-ray films were taken October 7, 1947. The films revealed the fetus to be lying across the abdomen with the head on the right and the breech on the left. There was marked hyperextension of the cervicodorsal vertebrae. This unusual position is described by Knowlton as "Flying Foetus." It was decided to attempt external version and, failing conversion, to do an elective cesarean section. Two unsuccessful attempts at external version were made. On Oct. 11, 1947, classical cesarean section was done and the child was extracted with little difficulty. Exploration of the uterus revealed no tumors or abnormalities.

There were no apparent anatomic factors responsible for the abnormal attitude of the fetus. It is assumed that marked muscular spasm of the fetus was responsible for the etiology of this position. The child appeared normal in all respects except that it maintained the position of exaggerated hyperextension when placed on its side. X-ray films of the cervicodorsolumbar spine taken 4 days after birth, showed no defects or anomalies of the vertebrae. Six weeks after birth, the child had no evidence of the opisthotonoid attitude.

PERSPECTIVES IN PREMATURITY

Physiological Approaches to an Obstetric Problem

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Am. J. Obst. & Gynec., 58: 65, 1949

The physiological study of prematurity involves an understanding of the accommodation of the uterus to the products of conception. The main features of implantation of the ovum are well understood. The changes occurring in the uterus during gestation are very poorly understood.

Among the mothers over the age of 41 who had a mongoloid child, 43 living children had previously been produced. All these siblings were normal; many of them were exceptionally intelligent.

The most outstanding symptom in the age group of 31 to 40 was slow fertilization time. In this group 81% had a waiting time of 3 years or more and 62% waited from 5 to 12 years for the birth of a child which was frequently the first or second one. In this group bleedings during pregnancy occurred in almost half the cases. The 48.8% of hemorrhages is far greater than the figures on threatened abortion in the general population given by Rutherford (4%) and Paine (3.8%). Indication of hormonal abnormalities is further given by the high percentage (47.6%) of menstrual irregularities in this group before pregnancy. The mothers of mongoloid children between 21 and 40 years of age had known thyroid dysfunction in 38.5%. This increased incidence of thyroid dysfunction in mongolism has also been observed by Myers and Hoskins.

Among the mothers who had a mongoloid child in their twenties, thyroid disorders, relative sterility, bleedings during pregnancy, and an irregular menstrual history, are also observed in a significantly high incidence of cases. Thyroid disorders occurred in 38%, difficulty in becoming pregnant in 46%, bleedings during pregnancy in 38.5%, and previous abortion in 38.2%.

The author feels that the main problem of mongolism is its prevention. The present study offers new evidence that mongolism is due to an abnormal maternal condition during the early part of gestation.

distribution and amount of extracellular fluid. It is the time, moreover, when the toxemias of pregnancy begin to make their appearance with some degree of frequency and are seen more often from then on. Since Reynolds is able to correlate the phenomenon of conversion with alterations in the rate of blood flow through the uterus, and since uterine ischemia is widely held to play a role in the causation of the toxemias, material is afforded here for endless speculation upon the possible relationships between conversion, uterine blood supply, resultant changes in the extracellular fluid and the development of toxemia. At the present writing all this may seem quite fanciful but here, at any rate, is a brand new concept and a phenomenon which might conceivably produce widespread alterations in maternal physiology.—Ed.)

PRENATAL MATERNAL FACTORS IN MONGOLISM

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J. A. M. A., 139: 979, 1949

This study deals with maternal conditions leading to the abnormal development of the embryo. The author believes that the causative factor in mongolism is either of a genetic nature, or else it is an environmental one.

In previous studies Benda has shown that mongolism is not due to genetic factors because mongolism increases in proportion to advanced age of the mother. Moreover, in large sized families the mongol is always found at the end of the line of siblings. The author has previously offered the theory that mongolism develops under a "threshold condition of hormonal sterility" in which the maternal organism appears to be unable to produce the proper endocrine environment for the embryo. The maternal condition is due either to the approach of the menopause, an insufficient response to fertilization, or an intercurrent illness which may render the mother temporarily unfit for a pregnancy.

Mongolism afflicts 3 children in every thousand births. The author studied 50 cases in 54 interviews. Four instances of relatively young women were excluded because no explanation could be found. An additional 10 cases were examined but were not included in the statistical evaluation. Eight of these 10 patients had a definite history of difficulties during one or more pregnancies.

The author believes mongolism is not a malformation or monstrosity but a deceleration of normal growth during the period of the 6th to 14th week of intra-uterine life. There cannot be one uniform cause because the constellation of causative factors differs in various age groups.

In the age group of 40 to 52 years, over 50% of the patients were actually in the menopause and pregnancy occurred against expectation. Of the 13 women above 40, 4 were above 45 and 3 had actually stopped menstruating completely.

Any normal mother is potentially the mother of a mongoloid baby, if she is approaching the menopause or carries her child under certain adverse conditions.

The discovery of the agglutinin P and its variants, as well as the known existence of variants of each of the Rh sub-types, promises an even greater individualization of human blood in the future.

MATERNAL MORTALITY IN HAWAII

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Hawaii M. J., 8: 267, 1949

The author recognizes that maternal mortality figures from a small population such as that of Hawaii, may be relatively insignificant. A 10 or 20 year analysis is not possible because of the lack of uniform record-keeping. This material, therefore, covers only 5 to 7 years. The maternal mortality in Hawaii has declined in a manner similar to that observed on the mainland. Ninety per cent of mothers in Hawaii in 1944 were delivered in a hospital, as compared with 77% on the mainland. For the 4 year period 1941 to 1945, Hawaii ranks 21 among the states and territories. It is well above states of a similar climate in regard to maternal mortality, indicating that a warm healthful climate does not counter-balance other factors.

For the years 1941 to 1945, hemorrhage and accident associated with hemorrhage were the greatest cause of maternal death in the Territory, with a rate of 0.7 as compared with 0.4 in the mainland. Ninety-five per cent of the deaths occurred during childbirth and the puerperium. The death rate from toxemia is exactly similar to that on the mainland, being 0.6. One half of all maternal deaths in Hawaii are due to eclampsia. Intrapartum and puerperal infection has a rate of 0.4; abortion 0.2. During the period under discussion, only 2 deaths occurred in Hawaii from ectopic pregnancy. In Honolulu, deaths due to toxemia are the greatest cause of maternal mortality, with hemorrhage ranking second. For the territory as a whole, hemorrhage is the greatest cause of death, and toxemia is second.

The author recommends that hemorrhage should be attacked by the provision of an adequate blood bank, avoidance of ill-advised meddling during labor, and having well trained obstetricians act as consultants. Toxemia fatality rates may be reduced by careful prenatal care.

SOCIAL AND LEGAL ASPECTS

MEDICOLEGAL ASPECTS OF THE Rh-Hr BLOOD TYPES

ALEXANDER S. WIENER

Bull. New York Acad. Med., 25: 255, 1949

For medicolegal work, all blood tests should be done preferably in quadruplicate, using as controls blood specimens of known groups and types. The agglutinogens A and B cannot appear in the blood of a child unless present in the blood of one or both parents. Group AB parents cannot have group O children and group O parents cannot have group AB children. Agglutinin A may be subdivided into A1 and A2. Numerous other variants of B probably also exist but are not well defined. No child can belong to subgroup A1 or subgroup A1B unless one or both parents belong to one of these subgroups. Parents of subgroups A1 and B cannot have children of subgroup A2 and parents of subgroup A2 cannot have children of subgroup A1B.

In the ordinary medicolegal case, the mere fact that blood groups correspond does not prove parenthood, and a putative parent can be established as innocent in only about one case in 6.

The agglutinogens M and N cannot appear in the blood of a child unless present in the blood of one or both parents. Type M parents cannot have type N children and type N parents cannot have type M children. With the combined use of the M-N types and the A-B-O groups, the chances of excluding paternity where a false accusation has been made, are raised from 16% to approximately 30%.

Three Rh factors exist: Rh₀, Rh', and Rh". The first of these is by far the most antigenic and the most common cause of clinical complications. In most clinical laboratories, the tests are confined to anti-Rh₀ serum alone. There are 3 Hr types corresponding to the three Rh types. For medicolegal use most experts have available anti-serum of specificity Rh₀, Rh', Rh", and Hr'. A few also have anti-serum of specificity Hr". Anti-serum of specificity of Hr₀ is still not available for general use.

Factors Rh₀, Rh', Rh", Hr', and Hr" cannot appear in the blood of a child unless present in the blood of one or both parents. Hr' negative parents cannot have Rh' negative children, and Rh' negative parents cannot have Hr' negative children. Hr" negative parents cannot have Rh" negative children and Rh" negative parents cannot have Hr" negative children. The discovery of the Rh-Hr blood types has resulted in an increase in the chances of exclusion for a falsely accused man to about 55%.

The writer has studied 450 cases. In 31 of these, paternity was excluded by the Rh-Hr test. In 14 of these, paternity was also excluded by the A-B-O tests, the M-N tests, or both.

hemorrhage, once in 200 cases, calls to mind the fact that claims about postpartum hemorrhage should not be made unless the blood loss has been accurately measured. If this is done, it will be found well nigh impossible to run 100 consecutive cases by any means without at least one or two cases in which the blood loss exceeds 500 cc., the most acceptable borderline for postpartum hemorrhage. It is doubtless true that caudal anesthesia gives less postpartum hemorrhage than ether, but the figure of 0.5 per cent leaves me skeptical. —Ed.)

CONTINUOUS PERIDURAL AND CAUDAL ANALGESIA IN OBSTETRICS

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Current Researches in Anesth. & Analg., 28: 61, 1949

Dangers to the life and cortex of the child, inherent in general methods of obstetric analgesia, may be avoided by carefully controlled regional methods of analgesia. In 1933, the author presented a method of completely abolishing the pains of childbirth by accurate paravertebral and caudal block of the pain pathways. Largely as a result of Hingson's efforts, continuous caudal analgesia is now used in more than 1,000 clinics in the United States. Spinal anesthesia, stimulated by the work of Adriani, is used in many other clinics. Hingson estimated that more than half of the 125,000 potential citizens dying at birth every year in the United States, could be saved by the universal adoption of regional anesthesia.

The chief objection to regional anesthesia has been the need for constant trained supervision from the time it is started until delivery. To abolish the cramping pain of labor, it is necessary to block the pain pathway entering the spine at the 11th and 12 thoracic roots; to abolish the pain of distention, a caudal block need go no higher than sacral roots. When enough anesthetic is injected to ensure relief, it may rise above the 11th thoracic root to involve the lesser splanchnic and greater splanchnic nerves which maintain the blood pressure. If the systolic blood pressure is permitted to fall below 75 mm. of mercury, the intrauterine pressure then exceeds the pressure of blood to the baby. Constant observation of the blood pressure is absolutely essential.

The necessity of constant supervision may be avoided by paravertebral block of the 11th and 12th thoracic roots, followed by low caudal block when pain of distention is felt. Of the various anesthetics tried, the longest relief was given by nupercaine 0.4% with adrenalin 1/100,000. After comparing the records of the effects of 200 paravertebral lumbar sympathetic blocks with 200 paravertebral thoracic blocks of the uterine sensory nerves, it was decided that the ideal method for routine use would develop from the latter by perfecting the approach to the more superficial 11th and 12th thoracic roots. It was found

OPERATIVE OBSTETRICS

CAUDAL ANESTHESIA IN OBSTETRICS: A COMBINED PROCAINE-PONTOCAINE SINGLE INJECTION TECHNIC

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Anesthesiology, 10: 473, 1949

In 200 obstetrical cases, the authors used a procaine-tetracaine combination as the anesthetic agent in caudal anesthesia at the end of the first stage of labor. Pontocaine hydrochloride was employed in all cases. The decreased time interval between the completion of the injection of the anesthetic agent and the complete relief of pain obtained with a procaine-tetracaine solution makes this the ideal anesthetic mixture for caudal injection. Relief of pain occurs in one to 5 minutes after injection, and the duration is usually from 2 to 5 hours.

Primiparas were anesthetized at the end of the first stage of labor, and multiparas when dilatation was 7 to 8 cm. Seconal was given before the anesthesia to help combat any possible reaction to the cocaine derivatives to be injected. The authors recommend the use of a test dose of 8 cc. and waiting an interval of 5 minutes. The patient is then given the remaining 22 cc. of the solution. The entire anesthetic agent contains 1.5% of procaine (450 mg.), and 0.15% of tetracaine (45 mg.). The volume of solution used varied between 28 cc. and 33 cc. A level of from the eighth to the eleventh thoracic segment is obtained with a volume of 30 cc.

The need for catheterization was not increased with terminal caudal anesthesia. Postpartum hemorrhage occurred in only one case (0.5%) and was associated with a low implantation. The incidence of manual rotation or Scanzoni maneuvers was not increased to any marked degree. Very little change in blood pressure was encountered. Sensitivity to the anesthetic agent was demonstrated in one case.

The authors believe that this is a very satisfactory method of obstetrical anesthesia for the busy obstetrician or for those who lack adequately trained personnel for the continuous caudal method.

(It will be recalled that the term "tetracaine hydrochloride" is the official U. S. P. designation for the drug marketed under the name "pontocaine hydrochloride" and in the above article the two terms are used synonymously. The authors are giving their patients, it may be noted, what amounts to a double anesthetic. Thus, in most cases of single injection caudals which have been reported with procaine alone, the dosage has been from 300 to 500 mg.; and similarly, with pontocaine alone, the average amount used for single injection caudal has been about 45 mg. The mixture given the above patients contained both these doses. While this procedure has proved satisfactory in the 200 cases reported, it should be pointed out that the vasomotor effects of the two drugs when given together are doubtless additive and that a smaller dosage would be safer. The very low incidence of postpartum

(This article is an impressive example of the extent to which some workers are going to provide optimal pain relief in labor. Cleland is one of the pioneers in this field, having been the first in the United States to recommend paravertebral block in obstetrics. Because of his extensive experience and special skills, his own employment of the dual catheter technique recommended in the above paper is doubtless highly effectual and also simple. However, it requires two different types of needle insertion, either one of which is decidedly more difficult than the introduction of a spinal needle; and it would be my reaction that the results would have to be utterly superlative to merit adoption by obstetricians at large. "A specialist" someone has said, "is a man who takes an easy subject and makes it difficult." —Ed.)

ANESTHESIA FOR CESAREAN SECTION

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South. M. J., 42: 520, 1949

The ideal anesthetic or analgesic for cesarean section has not been found. The factors to be sought in a good anesthetic for section are: pain relief with minimum disturbance to normal physiologic function, safety to the mother and the fetus, and efficiency for the operator.

The author reports 1,104 cesarean sections by one anesthetist with one surgeon in 793 cases, with a second in 159, and with 31 different operators in 152 cases. A total of 986 patients received general anesthesia; 745 patients were given combinations of nitrous oxide, cyclopropane, ether, oxygen with premedication of "nembutal" or "seconal," varying from $\frac{1}{2}$ to 3 grains orally one hour before operation. Atropine sulfate from 1/400 to 1/100 was given intramuscularly 45 minutes before operation.

In the author's experience, inhalation technics are preferred. Any standard anesthesia apparatus with absorption attachment is used. Nitrous oxide is turned into the system at a flow rate that will cause the bag of the apparatus to be nearly half full when the 3rd inspiratory breath is taken. This gas is then closed off, oxygen to fill the bag to approximately seven-eighths full is flushed in by by-pass, and the cyclopropane is admitted at a flow of 1,000 cc. per minute. The cyclopropane flow is not changed until the patient is in the 3rd stage. The oxygen flow is left at a rate of 400 cc. per minute throughout the anesthesia. As soon as the patient is asleep, the cyclopropane flow is reduced to between 400 and 200 cc. per minute. At the end of $3\frac{1}{2}$ to 4 minutes, a rubber Guedel airway is inserted. When about 5 minutes have elapsed, the absorber for carbon dioxide is turned on. After about 6 minutes, the patient is usually ready for incision. In this series, the infant usually has been delivered within the first 3 minutes. After delivery of the infant, ether is added to the mixture in that amount which is carried into the circuit with oxygen and cyclopropane flowing at a total amount of 600 cc. per minute. If the transition to ether is smooth, the cyclopropane is

clinically, and verified by internal hysterography, that relief could be started earlier, without interfering with the normal course of labor, by the thoracic approach.

The clinical impression, gained by comparing 400 paravertebral and 600 continuous caudal blocks in labor, that uterine motor activity is relatively impaired when the lumbar roots are blocked, was confirmed by hysterography. It was deduced that the prolongation of labor that may result from too early, as well as too high, administration of midcaudal block may be avoided by substituting a localized block of the 11th and 12th thoracic roots. Leaving the lumbar roots intact enables the patient to get on her feet in early labor, and to bear down well in the second stage.

Pain relief could be maintained with paravertebral block alone, usually until dilatation was complete. If the low caudal block could be deferred until less than one hour before delivery, the normal reflexes of labor could be preserved for more spontaneous rotations of posterior positions and more normal deliveries. It was found that less than half the estimated initial dose for midcaudal block would suffice to relieve all pain with paravertebral block in effect. Thus, not only the possibility of affecting blood pressure or motor nerves regardless of the anesthetic used, but also the danger of fall in blood pressure from toxic absorption was removed.

It was conceived that if suitable apparatus could be devised, the need for giving the midcaudal dose with its professional supervision could be eliminated, if one had another catheter inserted peridurally between the 11th and 12th thoracic roots. In this way, the contraction pains could be controlled by the nurse with minimal dosage. The author used 2 catheters: one into the peridural space and one into the caudal canal. As little as 3 to 4 cc. of intracaine, 2% in 2% potassium sulfate in Ringer's solution and adrenalin 1/100,000, give the best results for peridural block. As for caudal block, as little as 10 cc. of intracaine will block the birth canal.

Since the evolution of this technique, no fall of blood pressure sufficient to affect the fetal heart has been observed. If analgesia from the test dose does not center below the umbilicus, the catheter should be withdrawn the distance of the same number of spines as it is segments too high. When peridural block is well localized in the 11th and 12th thoracic roots, this technique approaches the accuracy of sensory paravertebral block, with less volume of anesthetic.

Hysterographs showed that high caudal block arrested early labor; whereas painless contractions under peridural and low caudal blocks were undiminished. In late labor, midcaudal block did not arrest labor, although contractions were less strong than those under peridural or without block. Relief can be given earlier in labor by peridural block than is possible with caudal block.

With 2 catheters, the possibility of having to resort to a general anesthetic is remote. Success is more certain with peridural block than with caudal block as anomalies occur more frequently in the sacrum. For operative delivery in anomalous sacra, where a midcaudal injection cannot be given, a spinal saddle-block is indicated.

mortality rate from 1938-1942 was 56.2 per 1,000. For the second 5 year period, it was 85 per 1,000.

The author concludes that caudal anesthesia is the anesthetic of choice in obstetrics if there is a full knowledge of its inherent dangers and the manner in which they may be avoided.

(Although the author concludes that caudal anesthesia is the anesthetic of choice in obstetrics, the maternal and fetal mortality rates reported in the above abstract would not seem to justify of themselves any such claim. Thus the maternal mortality which could be attributed to anesthesia was about the same in the two periods as was likewise the total fetal mortality rate. In the premature group the results were actually worse for the second five-year period.—Ed.)

discontinued. On beginning the fascial suture, all agents except oxygen are discontinued and the absorber circuit is discontinued. With the start of the skin suture, the mask is removed. The airway is left in place until the first sign of reaction.

When spinal anesthesia was indicated, the technic described by Lapp was satisfactory. It consists of 3 grains of nembutal the evening before operation. Ten minutes before spinal tap, 50 mg. of ephedrine are given intramuscularly. Spinal tap is made in the 3rd lumbar space using 50 mg. of procaine and varying the pontocaine from 5-10 mg. as indicated. For any sudden drop in blood pressure, $\frac{1}{2}$ minim of "neosynephrin" has proved adequate.

The author concludes that the only limitation to the use of any agent or technic is the knowledge and dexterity of the anesthesiologist. Teamwork and individualization of each case are essential to success in anesthesia for cesarean section.

OBSTETRICAL ANESTHESIA AT THE CEDARS OF LEBANON HOSPITAL. A TEN-YEAR SURVEY

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West. J. Surg., 57: 169, 1949

The author reviews the obstetrical anesthesia at the Cedars of Lebanon Hospital from 1938 through 1947. During the first 5 year period, inhalation anesthesia was used in the majority of cases. During the second half of the period conduction anesthesia was used, mainly caudal. Recently, there has been an increase in the number of low spinal anesthetics.

For 9,884 deliveries from 1943 through 1947, 6,970 caudal anesthetics, an incidence of 70.5%, were given. In the pre-caudal group, 1938-1942, there were 5,527 deliveries with 9 deaths, a maternal mortality of 16.2 per 10,000. Only 3 of these could be connected in any way with the anesthesia. In the second half of the series, there were 9,884 deliveries and 10 deaths, a maternal mortality rate of 10.1 per 10,000. Six of these deaths were either caused by, or could have been caused by the anesthesia. Three of these 6 received a caudal plus chloroform.

In the first group, there were 170 stillbirths and neonatal deaths in 5,527 deliveries, a fetal mortality rate of 30.8 per 1,000. The comparative 5 years with conduction anesthesia shows 316 stillbirths and neonatal deaths in 9,884 births, a fetal mortality rate of 31.9 per 1,000. Intrapartum deaths and neonatal deaths under 7 full months' gestation were deleted.

The premature fetal mortality rate was compiled from among those babies delivered between 7 and 9 months of gestation. The corrected premature fetal

CRIMINAL ABORTION AND INTESTINAL DESTRUCTION

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West J. Surg., 57: 163, 1949

The authors report the case of a woman upon whom a criminal abortion was performed. The uterus was perforated and the intestine pulled down. The abortionist cut the intestine off, thinking it was umbilical cord.

Laparotomy under spinal anesthesia was performed immediately upon the patient's arrival in the hospital. The patient was not in shock. The uterus was enlarged to the size of a 2½ month pregnancy. There was a perforation just anterior to the right cornu. The ileum had been removed for a distance of 30 inches—the distal cut having been 6 inches proximal to the ileo-cecal valve. The mesentery between the cut ends contained the serosa of the excised bowel. There was very little arterial bleeding. The cut ends of the ileum were closed and a side to side anastomosis done. The rent in the uterus was repaired with 3 mattress sutures of 00 chromic catgut.

The patient had a perfectly smooth and uneventful postoperative course. She did not abort. The patient was lost sight of before her pregnancy came to term.

MISCELLANEOUS

DEATH FROM ATTEMPTED ABORTION WITH A POTASSIUM PERMANGANATE DOUCHE

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New England J. Med., 240: 794, 1949

Potassium permanganate is rarely a cause of fatal poisoning when ingested. Within recent years, potassium permanganate (0.3 to 1.0 gm.) tablets have been used as an abortifacient, mostly in Europe, but also in this country. Bleeding usually follows about 2 hours after the insertion of the tablet; suture of bleeding points and vaginal packing are often necessary.

The authors report the first case in which death has followed the use of potassium permanganate as an abortifacient. A 21 year old single woman used a saturated solution of potassium permanganate containing at least 7 grams of the chemical as a douche. She entered the hospital in a state of acute collapse and died 8 hours later. At autopsy, the entire skin was a uniform brown in color. The cervical os was one centimeter dilated. The inner aspect of the uterus showed diffuse superficial hemorrhagic necrosis and no evidence of the fetus could be identified. Microscopically, the disorganized remains of a decidual reaction could be identified. The decidua and myometrium were focal and confluent hemorrhagic extravasation. In the cervix there was a marked perivascular polymorphonuclear infiltration. Microscopically, the kidneys showed numerous pigmented casts, chiefly in the lower portions of the nephron.

Manganese was detected in the uterus and the blood by spectrographic examinations. After centrifugation, the blood serum was dark brown. This was due to the presence of a pigment which has been identified as alkaline met-hemoglobin.

Potassium permanganate causes local injury because it is a strong oxidizing agent. In addition, potassium hydroxide is produced by combination with tissue fluid and secondary potassium hydroxide penetration may take place. Permanganate introduced into the circulation, as must have occurred in this case, may act as an acute hemolytic agent. Both hemolysis and pigment formation are caused by the strong oxidizing agent. With rupture of the red cell, the hemoglobin is freed and is instantly oxidized to met-hemoglobin. Hyperpotassemia due to local absorption of potassium ions and potassium ion release incident to acute hemolysis may also occur.

the egg as it passes down the tube. However, the desquamated follicular cells may pass down the tube following the ovum and be directed to the same spot as the ovum by the same currents which influence the ovum to implant there. There are many published reports of the tenacity of the cumulus cells in adhering to the egg. Hyaluronidase, when added to the uterine horns of rats, was not able to denude the ova therein contained.

The author believes that the endometrium is the source of pregnancy gonadotrophin which is secreted for the purpose of maintaining the trophoblast. This would explain why "chorionic" gonadotrophin has no effect upon the human gonad and is worthless in gynecological therapy. In the case of extra-uterine pregnancy, the author believes that ectopic endometrium elaborates gonadotrophin.

This theory might be approached in several ways. The agglutinogens of the trophoblast should be absorbed. If agglutinogens, not present in the mother, are found, the trophoblast must be of fetal origin. (The mesodermic core of a villus is certainly fetal in origin, so in order to be certain that this error does not arise, no fetal mesoderm must be present. Probably the chorionepithelioma is the only tissue that meets these tests.) A further experiment would be to transplant follicular tissue to the uterine endometrium and stimulate it to grow with gonadotrophin. One would then expect, if the correct gonadotrophin is used, to see trophoblast develop.

(I believe that the reaction of every embryologist, gynecological pathologist and endocrinologist who reads this paper will be one of surprise and irritation. It abounds in statements which are not only highly unorthodox but which are quite surely incorrect. The opening paragraph of the abstract, stating that the placental trophoblast is derived from the granulosa cells which adhere to the ovum when it leaves the ovary, expresses the author's chief thesis. One can imagine the universal lifting of eyebrows among the embryologists who read this statement, which puts them all out of step with the maverick author of this paper. The latter's concept, it should be said, is not based upon any personal observation or study, but has apparently been evolved by what appears to be a twisting, at times rather violent, of many scattered observations, not always established, to prove what is apparently an *idée fixe*. While I am convinced of his sincerity, his contribution impresses me as a rather perfect example of sophistry.)

The origin of the human trophoblast from the embryonic ectoderm has been established beyond doubt, and this tenet is, indeed, one of the cornerstones of embryological knowledge. Many of us have seen the moving pictures of the fertilized rabbit egg which were made by Warren Lewis a good many years ago, and which showed the segmentation of the egg, from which incidentally all trace of the originally adherent granulosa cells had disappeared, with differentiation of the embryonic cells into those of the primitive trophoblast. Even more convincing evidence on this point is readily available in the studies of Hartman and others on the very early fertilized eggs of the monkey, and the now classical contribution of Rock and Hertig upon very early human eggs.

As to some of the other "evidence" mentioned by the author, I do not think that many will accept the statement that the endometrium produces chorionic gonadotrophin. While I suppose that it would be difficult to exclude altogether the possibility that other tissues than the trophoblast may contribute to the formation of this gonadotrophe, there is no doubt that the chief and possibly the only source is the trophoblast. A crucial demonstration of this was the recovery of this hormone from pure tissue cultures of trophoblast by

Gynecology

ENDOCRINOLOGY

THE ORIGIN OF PLACENTAL TROPHOBLAST AND THE FUNCTION OF PLACENTAL GONADOTROPHIN

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Lancet, 1: 807, 1949

The author believes that the main portion of the placental trophoblast is derived from the granulosa cells which surround the ovum when it leaves the ovary.

Both the placenta and the ovaries secrete estrogen and progesterone as well as androgens. The ovary is known not to produce a gonadotrophin; but the author points out that there is considerable evidence (Fellner, Catchpole and Lyons, Cole and Goss) that the endometrium produces "chorionic" gonadotrophin.

The trophoblast is not part of the fetus for it may exist independently of the fetus, as in hydatid mole. Moreover, the placenta survives even after the death of the fetus. Although chorionepithelioma is a tumor of the trophoblast, it can exist without previous fertilization of the ovum. The occurrence of chorionepithelioma in old women, virgins, and men is also difficult to explain on the basis of fetal origin. The author feels that chorionepithelioma results from metaplasia of the granulosa.

Granulosa cell tumors arise in the ovaries which have been transplanted in castrated rodents. This is due to a hypersecretion of gonadotrophin by the pituitary gland which is no longer under the control of estrogens. It illustrates, however, the malignant potentialities of granulosa cells.

Only in the higher mammals is the graafian follicle divided into 2 portions so that part of the granulosa is extruded with the egg. This type of follicle has arisen in phylogeny with the development of invasive trophoblast.

The granulosa layer and the trophoblast have analogous functions. The follicular epithelium provides for the protection and nutrition of the ovarian egg; the trophoblast serves in a like capacity to the embryo. The cytotrophoblast and chorionic epithelium in man are histologically dissimilar, even in the early pre-villous stages.

Transportation of trophoblastic elements is a well known phenomenon in pregnant females. On the other hand, transplants in general, among the higher mammals, are usually unsuccessful. These facts favor the maternal origin of the trophoblast.

Numerous investigators have stated that the cumulus oophorus is shed from

No evidence was obtained in this series to indicate that testosterone propionate had any specific inhibitory effect on advanced carcinoma of the breast, that it altered the course of the disease, or that it resulted in any improvement in the survival rates obtained by the more commonly accepted forms of therapy.

(The conclusions of the authors from the study of this small group of cases, as expressed in the last paragraph of the abstract, conform to those arrived at by others in the study of much larger numbers. The most extensive investigations on this point are those being carried out by Adair at the Memorial Hospital. While no curative effects are claimed, I believe that it is the feeling of the Memorial Hospital Group that the frequent relief of pain and the lessened discomfort of the patient appear to warrant a continuance of the plan. It must be remembered that no benefit is to be expected unless very large dosage of testosterone is employed, so that unpleasant masculinization symptoms, especially unsightly hirsutism, are always to be expected.—Ed.)

ANTIHORMONE FORMATION DURING CHORIONIC GONADOTROPHIN THERAPY

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J. Clin. Endocrinol., 9: 384, 1949

The administration of gonadotropic extracts from heterologous sources frequently elicits antihormone formation in man, whereas homologous source material does not cause hormone antagonists to develop.

In order to assess antihormone formation in response to a highly purified chorionic gonadotropin, serum samples were obtained from patients receiving chorionic gonadotropin for a study of the hormone's effect on the functional life of the corpus luteum. The 2 to 3-fold increase in mouse ovarian weight induced by 20 I.U. of chorionic gonadotropin was completely prevented by concomitant administration of the patient's serum.

In the absence of any other hormone treatment, a highly purified chorionic gonadotropin excited antihormone formation. It is suggested that the manipulation necessary to gain purity may have altered the hormone so that it could be antigenic in the large amount (760,000 I.U.) administered.

(It has been a good many years since Collip evolved the concept of antihormones. At the time it was a rather startling one, and many thought that it might well apply in the explanation of the frequent inefficiency of organotherapy. On the whole it cannot be said that the doctrine of anti-hormones has influenced endocrine therapy greatly, and there is still much uncertainty and difference of opinion among investigators as to the specificity or non-specificity of anti-hormonal reactions when they occur. Probably the most valuable endocrines in gynecological practice are the estrogens and thyroid and, so far as I know, no evidence has been adduced to indicate that their administration evokes the production of anti-hormones, and the same statement would seem to apply to progesterone and the an-

Gey, Hellman and Jones a good many years ago, with later confirmation by other investigators.

The trophoblast of a hydatidiform mole has its origin from the covering of the chorionic villi, as every gynecological pathologist will testify. It is true that portions of the trophoblast can break off and find their way into the blood vessels and thus to the lungs, where they can exist for a limited time independently, but this certainly does not negate their origin from the embryonic trophoblast. Such trophoblast, like the trophoblast in a tubal pregnancy, can survive, but only for a limited time, after the somatic death of the embryo from which it arises. As for the fully formed placenta, surgeons know well enough that, in cases of secondary abdominal pregnancy, there is a big difference between the vascular and functioning placenta in those cases in which the fetus is still living and the retrogressed non-functioning placenta associated with a fetus which has long since succumbed. Again, the occurrence of chorionepithelioma in old women, virgins and men is no more difficult to explain than is the presence of skin or bone in the teratomas to which the author evidently refers. The ectodermal trophoblast, like the ectodermal skin, is a fetal tissue, which brings us right back to where we started from.

Another shining target set up by the author is his statement that "chorionepithelioma results from metaplasia of the granulosa," but why go on? I suspect that I have conveyed the general idea that I do not agree with most of the author's conclusions, nor with the manner in which these conclusions were reached. I do not believe that a full reading of his paper will make many converts.—Ed.)

TESTOSTERONE PROPIONATE IN THE TREATMENT OF ADVANCED CARCINOMA OF THE BREAST

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Surg., Gynec., Obst., 88: 702, 1949

There has been little clinical evidence to prove that the administration of estrogens ever results in the production of cancer of the human breast or that the administration of androgens to patients who have cancer of the breast results in any permanent benefit. The authors used testosterone propionate in amounts up to 3900 mgms. to treat 7 patients with carcinoma of the breast. Four of the patients had operable carcinoma of the breast with proved axillary metastases; 2 had inoperable carcinoma with skeletal metastases; and one patient had recurrent carcinoma following previous radical amputation.

Systemic improvement consisting of a gain in weight and strength occurred in all cases, being most marked in those with the greatest debility. It appeared within 2 to 3 weeks of treatment, but was of temporary duration. The pain of bone metastases was relieved in the 2 patients who had such lesions. There is evidence that systemic improvement, relief from pain, and calcification of bone metastases are due to the anabolic effect of the drug on the entire body, rather than to any specific effect on tumor cells.

78 days. The cycle may be reinitiated by a single implantation; several cyclic bleedings may occur which are again followed by amenorrhea, requiring a second implantation, or even a third. The effect of implantation may be estimated by vaginal smear and by the examination of the uterine mucosa obtained by a diagnostic strip curettage. The dosage must vary with the severity of the clinical symptoms. Doses may range between 25 and 50 mgs. of estrone or estradiol. Doses higher than 50 mgs. should not be administered.

It must be concluded that the cyclic estrogen-progesterone withdrawal flow plays a physiological role in the cyclic pituitary-ovarian interaction. The present investigation demonstrated that the same effect may be obtained by continuous stimulation with estrogenic hormone flowing from the pellet reservoirs. Apparently, the central stimulation of the gonadotropic function of the anterior pituitary lobe combines with the peripheral stimulation of the ovary, sensitizing the latter to the influence of pituitary gonadotropin. As a result, the central mechanism, that of the anterior pituitary as the motor of sexual function, appears to be reinitiated.

(With all due respect to the eminent senior author of this paper, who has made such fundamental contributions to reproductive endocrinology, and in spite of the three advantages which he enumerates for the method of intravaginal implantation of estrogen pellets, it is difficult for me to believe that this could be expected to yield results materially different from those of long continued oral estrogen therapy. For example, the authors report the average interval between vaginal implantation and the onset of bleeding as seventy-eight days, but surely such bleeding can often be induced much more quickly by adequate oral estrogen therapy. The necessity for proper regulation of the dose as the authors themselves emphasize is no less real with the vaginal than with the subcutaneous or oral routes, especially as one is constantly dealing with the rather intangible factor of individual sensitivity or refractoriness of the recipient endocrine glands. The authors are undoubtedly correct in their view that the cyclic estrogen-progesterone withdrawal flow plays a role in the cyclic pituitary-ovarian interaction, but it is of interest to note that they utilize estrogen alone in their efforts to re-establish a normal mechanism. This as a matter of fact, has long been my own impression. There are many who believe that the sequential use of estrogen and progesterone, in imitation of the normal menstrual mechanism, is more likely to reawaken the cyclic gonadotrophic pituitary mechanism than the employment of estrogen alone. On purely clinical grounds, this has not been my own observation, and I have for many years employed estrogen alone for this purpose, though concededly with anything but brilliant results. So far as I can see, the estrone-progesterone plan has likewise not seemed to be the answer to the problem, though the important work of Zondek has intensified interest in the progesterone withdrawal plan of treatment. The scientific standing of the authors of the paper abstracted above warrants serious consideration of the vaginal implantation management they propose, but I confess to a feeling of dubiousness as to whether it will satisfactorily answer our therapeutic problems in cases of amenorrhea and endocrine sterility.—Ed.)

drogens. It is the gonadotrophes which have apparently been chiefly culpable in this respect, and the fact that gonadotrophic preparations, even those which are purified, contain at least some trace of protein, has led many to believe that the supposed anti-hormonal effects are really evidences of protein reactions. Zondek and his co-workers hold such views, as do others, but there are also good investigators who believe that the reactions are specifically anti-hormonal. Whether the studies of the authors of the paper abstracted above with a "highly purified chorionic gonadotropin" constitute any convincing evidence on these matters, I do not know. Probably the question will not be conclusively resolved until we know more about the chemical structure of the gonadotrophes than we do now.—Ed.)

STIMULATION OF OVARIAN FUNCTION AND INDUCTION OF PREGNANCY THROUGH INTRAVAGINAL IMPLANTATION OF ESTROGEN PELLETS

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Surg., Gynec. & Obst., 88: 783, 1949

The problem of amenorrhea plays a very significant role in the treatment of sterility. Amenorrhea may be the symptom of a general disease, or it may be the result of psychic or climactic factors. However, many cases of amenorrhea are of endocrine origin, reflecting a disturbance in the pituitary-ovarian relationship.

The authors treated 62 women with amenorrhea by intravaginal implantation of estrogen pellets. Seven of the patients suffered from primary amenorrhea and 55 patients had secondary amenorrhea of 2 to 10 years' duration. Of these 62 patients, 52 responded with bleedings and 38 reported several cyclic bleedings following a single implantation; 26 patients had regular bleedings up to 12 months. In 12 cases, the cycle was completely established, and 8 of these women became pregnant. All of the patients had been unsuccessfully treated for extended periods of time and had unpromising prognoses. All of the patients exhibited marked degeneration of the genital organs. Sterility had lasted for 3 to 7 years.

Intravaginal implantation possesses the following advantages over subcutaneous administration: (1) the effect is more constant, (2) the effect is about 5 times as intense, and (3) the tablets are seldom expelled. An effect sometimes associated with this method of treatment is an excessively intense peripheral reaction involving glandular cystic hyperplasia of the uterine mucosa, sometimes accompanied by severe bleeding. Excessive bleeding may be avoided if not more than 30 to 40 mgms. of estrogen be implanted.

The effects of the estrogen implantation were manifested in improved vascularization of the vagina, in changes in the vaginal epithelium, in uterine growth, proliferation of the uterine mucosa, uterine bleeding and enlargement of the breasts. The average interval between implantation and the onset of bleeding was

THE MENSTRUAL CYCLE

PRECOCIOUS PUBERTY IN GIRLS

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Virginia M. Month., 76: 303, 1949

It is suggested that the normal time of sexual development is tied up genetically with maturation of the hypothalamus and the hypophysis. At puberty, a hypothalamic-hypophyseal mechanism comes into play which either stimulates the pituitary to gonadotropic secretion or removes inhibitions to secretions which were present during immaturity. The chain of events, resulting in puberty, normally occurs between the years of 9 and 17. If puberty occurs before the age of 9, it is said to be precocious.

TABLE I
Precocious Puberty in Girls
Classification of Cases (Modified from Seckel)

I. Constitutional
(Chromosomal or genic basis. Hypothalamic level. No lesion.)
II. Pathologic
A. Cephalic (Various lesions, primarily or secondarily affecting the hypothalamus).
B. Abdominopelvic (Hormonal)
1. Ovarian
a. Granulosa cell tumor
b. Teratomas
c. Chorionepitheliomas
d. ? et al.
2. Adrenal-cortical
a. Neoplasms
b. Hyperplasias
III. Miscellaneous
A. Albright's syndrome
B. et al.?

Table I presents a classification of precocious puberty in girls. In the constitutional group, there is apparently a premature maturation of the hypothalamic sex centers due to an inherited factor. The cephalic group contains lesions which apparently affect the hypothalamus or the hypothalamic-hypophyseal mechanism by actual invasion or through pressure. No case of precocious puberty due to primary disease of the pituitary has been reported. The lesions in the abdominopelvic group primarily affect hormone-producing glands, thereby causing excessive endocrine secretion which brings about the sexual changes.

A NOTE ON THE ANTIQUITY OF THE ADRENO-GENITAL SYNDROME

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Bull. Hist. Med., 23: 201, 1949

The ancient Greeks recorded two instances of the adreno-genital syndrome. In Apid. VI, Sect. 8, 32, the following description was provided:

"At Abdera, . . . (a married woman) had had children previously; but her husband having fled, her menses became suppressed for a long time; afterwards, pains and redness in the joints . . .; the body assumed a masculine appearance, this woman became hairy all over, a beard appeared in her, the voice became rough; and in spite of all that we could do to restore the menstrual flow, it did not come; this woman died not long after. The same thing happened to . . . (a married woman) in Thasos; according to all the physicians that I met, the only hope of restoring her womanly attributes lay in the return of the menses; but in her also, despite all measures, the menses did not return; this woman soon succumbed."

It is interesting to realize that in its essential features the adreno-genital syndrome has remained fundamentally unchanged throughout the ages.

the constitutional or granulosa tumor cases, the clitoris is often greatly enlarged, and breast enlargement is absent. Instead of the precocious hair development being limited to the genital and axillary areas, there is often more or less hirsutism of the extremities, with sometimes tufts of hair on the chest and back, as well as a male pubic escutcheon. Finally, in only a small proportion of the adrenal cases is precocious menstruation included in the premature developmental manifestations.—Ed.)

HORMONAL CONTROL OF THE MENSTRUAL CYCLE— APPLICATION OF PHYSIOLOGIC CONCEPTS TO THERAPY

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Cincinnati J. Med., 30: 248, 1949

The normal menstrual cycle is characterized by phases of endometrial growth and regression, ovulation and bleeding from a progestational endometrium. During the bleeding phase, under the influence of FSH, the follicles produce estrogen. As the blood estrogen level rises, FSH is suppressed and LH is produced. The follicle is transformed into the corpus luteum which is maintained by LT and produces estrogen and progesterin. The rising levels of progesterin suppress the secretion of LT and the corpus luteum degenerates.

Estrogen causes growth of the endometrium; a 50% decrease in estrogen level will cause endometrial regression and bleeding. Progesterin prepares the endometrium to receive the fertilized ovum. If pregnancy does not occur, the corpus luteum degenerates and the endometrium regresses.

The average normal menstrual cycle is considered to be 28 days long. Unusually long or short cycles are generally due to variation in the pre-ovulatory, not the ovulatory phase.

The most common type of bleeding irregularity is called functional excess of bleeding. Acyclic excesses of bleeding usually occur from an estrogenic endometrium because of a disturbance of pituitary, ovarian, and endometrial rhythm. Cyclic profuse bleeding commonly occurs from a progestational endometrium and is organic in nature.

Studies of functional bleeding should include BMR determinations and, if the patient is over 35, a D & C, in addition to a careful history and physical examination.

If the patient is seen during an episode of profuse bleeding, hemostasis may be obtained by curettage. A simpler method is to give estrogens, 2.5 mg. three times a day. If bleeding does not decrease within 2 to 3 days, the dosage should be increased 50 to 100%. When bleeding stops, a cycle of estrogen and progesterone therapy is begun. The hemostatic dose of estrogen is continued for 20 days.

Usually the most outstanding sign of female precocious puberty is uterine bleeding. In the constitutional type, the precocity is isosexual and complete, and the bleeding is ovulatory. In this type, pregnancy can and does occur. In the cephalic type, the precocity is also isosexual and complete. Though pregnancy may be possible in these cases, it has never been recorded. In the abdominopelvic group, ovulation does not occur. Ovarian precocious puberty is isosexual and incomplete. Adrenal precocious puberty is incomplete and usually heterosexual.

There is a preliminary acceleration of skeletal growth in precocious puberty. Bony arrest occurs prematurely also. The mental growth of the patients does not keep pace with the somatic growth and, in general, is not influenced.

In the cephalic type, the urinary estrogens are within the normal adult range. In cases of granulosa cell tumor, the urinary estrogens are usually increased; in the adrenocortical group, the 17-ketosteroids are increased within or beyond the range normal for mature males. Urinary gonadotropins have generally been negative in all types of cases.

The majority of cases of precocious puberty are of the constitutional type. Granulosa cell tumor is the most common of the ovarian causes of premature puberty.

Where operable lesions are present, these should be removed. The prognosis in cases due to lesions of the brain is bad, whereas, in cases due to granulosa cell tumor of the ovary, it is excellent. Patients in the constitutional group should be studied and kept under observation for signs of organic disease. The patients in this group, as a rule, become essentially normal adults.

(This is an excellent review of the subject and the modified Seckel classification of precocious puberty given in Table 1 leaves little room for criticism based on our present knowledge. As the author implies, the 2 most important types from the standpoint of gynecological practice are the constitutional and that due to granulosa cell tumors. Since the gynecologist is apt to have read much more about the latter than the former, it should be emphasized that the constitutional variety is far more frequent than that due to ovarian neoplasm. This is not an unnecessary admonition, as a good many cases of female precocious puberty have been unwisely submitted to laparotomy simply because the surgeon wrongly theorized that a small ovarian tumor must be present even if it could not be felt.

Hoge has also called attention to the fact that the precocious menstruation seen with granulosa tumors is never associated with ovulation, the periodic bleeding being of purely estrogen-induced type. On the other hand the constitutional type, being due to the release of a perfectly normal puberty mechanism at an abnormally early period of life, is characterized not only by precocious menstruation but also as a rule by precocious ovulation. Such children, therefore, can become pregnant if inseminated, and there is little doubt that this has been the responsible factor in the now numerous reported cases of freakishly early motherhood, such as the earliest of all, that in the famous case of Lena Medina, the little Peruvian girl who was delivered by cesarean section at the age of 5½ years. It is obvious that the hazard of possible impregnation must never be lost sight of in the management of these constitutional cases.

As to the rare cephalic cases, these rarely come to the gynecologist's attention as the pubertas praecox symptoms in such cases are likely to be accompanied by or overshadowed by those more directly produced by the brain tumor or other lesion responsible for the disturbance. Again, as to the adrenal cases, these can usually be suspected on simple clinical grounds, chiefly the fact that the precocious symptoms are always heterosexual. Unlike

thighs. It evidences itself as a dull ache, and is frequently associated with nausea. Uterine pain is typically sharp, stabbing, cramplike or colicky.

The author found that sclerocystic changes in the ovary are very common in ovarian dysmenorrhea. In these cases there are often associated degenerations of the peri- and intra-fascicular ovarian nerves. The 2 determining factors are an existing nerve degeneration plus pressure upon either the ovarian intrinsic nerves or some fibrils adjacent to the granulosa cell layer of a follicle. The ovarian nerve supply is chiefly sympathetic and derived from the renal, intermesenteric, and celiac plexuses. There is a nerve cross-linked between the ovaries and successful denervation is necessarily bilateral. The author performs ovarian denervation by simple division of both infundibulopelvic ligaments, their nerves and blood vessels, and ligation of the stumps with catgut. To avoid elongation of the divided ligament with subsequent ovarian prolapse, the cut ends are carefully sutured to one another. In 21 cases of primary ovarian dysmenorrhea, the author had 17 successes, 3 failures, and one partial success.

Uterine dysmenorrhea was treated by pre-sacral sympathectomy. The pre-sacral nerve is usually a well-defined plexus lying retro-peritoneally in front of the last 2 lumbar vertebrae. The author performed presacral neurectomy in the usual manner, being sure to remove at least one inch of individual nerve fibers or of the plexus itself. In 27 cases of mixed ovarian and uterine dysmenorrhea, the author had 22 successes, 4 partial successes and one failure. In 34 purely uterine denervations, there were 25 successes, 5 partial successes, and 4 failures.

All the specimens obtained at operation were examined pathologically. The changes constantly observed may be summarized as: degeneration and destruction of sympathetic ganglion cells; degeneration of post-ganglionic fibers; and replacement fibrosis in the nerves. The author believes that the afferent nerves are first attacked. The ganglion cells are involved, and the post-ganglionic fibers consequently degenerate. The sensory fibers are secondarily implicated. Their sensibility is so altered that impulses from the uterus or ovary which normally are not unpleasant, produce pain.

The author's results lead him to believe that pre-sacral neurectomy and ovarian denervation do not endanger fertility. Labor following nerve resection was neither easier nor more difficult than the average. There have been no serious operative complications and the sexual life of the patients has not been disturbed.

The author believes that primary dysmenorrhea results from the prolonged celibacy which modern civilization has forced upon women, prior to marriage. He does not advocate promiscuity however.

(The paper abstracted above constituted the annual Joseph Price lecture delivered at the meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons in September of 1948. Its author is the present Headmaster of the Rotunda Hospital in Dublin, and is well known for the charming book which he has written concerning the history of that famous old institution. His paper on presacral neurectomy differs from most others on the subject in that he draws such a sharp line between primary dysmenorrhea of uterine and that of ovarian origin. The question at once arises, especially in view of our

During the last 10 days, oral progesterone is given. At the end of 20 days, all therapy is discontinued. Withdrawal bleeding may occur within a week. After 5 days of bleeding, a second cycle is begun. This cyclic therapy, repeated for 2 or 3 cycles, usually restores cyclic function.

Secondary amenorrhea may result from numerous causes. In addition to a complete general study, assay of urinary gonadotrophins and estrogens may be carried out. Amenorrhea resulting from hypopituitarism, ovarian failure, failure of other endocrine glands, or psychogenic disturbances, may be treated with cyclic estrogen and progesterone therapy. This treatment prevents premature senility, corrects metabolic deficiencies, acts as a psychotherapeutic tool, and may result in salvage of ovarian function.

(A simple but sound resumé of the subject which should be easily understandable and profitable to the general practitioners for whom it is chiefly intended, and many of whom are still sadly in need of instruction along this line. In her description of the hormonal control of menstruation the author includes no mention of luteotrophin but this is probably just as well. While it appears to be true, as Astwood first demonstrated, that luteotrophin is important in maintaining and activating progesterone, its exact role is still not altogether clear, and there is much reason to suspect its identity with prolactin.

While there are wide individual variations in the treatment of such quantitative menstrual disorders as amenorrhea and functional bleeding, the outline of management given by the author is a rational one and, in my opinion, as effective as any at our disposal.—Ed.)

A SURVEY OF 113 CASES OF PRIMARY DYSMENORRHEA TREATED BY NEURECTOMY

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Am. J. Obst. & Gynec., 57: 1053, 1949

The survey is based upon 113 healthy young women with primary dysmenorrhea. The latter was so severe as to incapacitate the patient every month. These patients were treated between the years 1936 and 1945. Eighty-two cases were followed up.

The author differentiates ovarian and uterine pain in dysmenorrhea. Bimanual compression of the ovary may produce pain resembling that experienced at the menstrual time. If this is the case, it is reasonable to suspect that the dysmenorrhea is of ovarian origin. In patients in whom the pain thus produced did not resemble that of menstruation, a sterile uterine sound was passed. The latter procedure produced typical uterine pain in 49% of the patients examined. In 11%, the passing of the sound produced typical referred pain in some other lower abdominal area.

Ovarian pain may be unilateral or bilateral; menstrual but chiefly premenstrual; always sub-umbilical, but chiefly left sided and radiating around the

onset of the pain was regular. The mean interval from menstruation to the onset of the pain is 17.3 ± 0.33 days, and from the pain to the beginning of menstruation 13.0 ± 0.15 days. The patient wished to become pregnant and was advised to regard the mittelschmerz as the most likely indication of the time of ovulation. Ten days after the mittelschmerz in that cycle, and before the next period was due, the patient correctly believed that she was pregnant. About 3 weeks after the end of lactation, the pain was again recorded, and was followed 10 days later by the return of menstruation. The pain has occurred 29 times on the right side and 14 times on the left.

A record of the daily waking oral temperature was kept for the last 13 cycles. An independent observer was asked to estimate the most likely time of ovulation from temperature charts alone. In 8 of the 14 cycles, ovulation, as judged in this way, agreed with the day of onset of the mittelschmerz. In 3 cycles, the estimate was one day early, and in 3, it was one day late. A change in the temperature curve is at best only indirect evidence of ovulation, but the close relation between the temperature change and the mittelschmerz is of interest.

Intermenstrual pain is obviously an indication of some alteration in the reproductive tract, and may be accepted as further evidence that ovulation occurs in the middle of the cycle. The cause of the pain is obscure. It is abolished by ovariectomy, but is not affected by operations that interfere with nervous pathways from the uterus. Painful tubal contractions may be a possible explanation. If the pain is connected with ovarian changes, the immediate cause may be either the pressure of a distending follicle just before ovulation or the actual rupture of the follicle. It seems probable that intermenstrual pain gives a closer indication of the time of ovulation, in those women who are aware of it, than any other method.

(This paper records an interesting observation and I am sure that many other gynecologists have seen an occasional case in which severe mittelschmerz has appeared to be the chief factor in the patient's sterility problem. When such pain is severe, coitus is likely to be avoided and at exactly the time when it would most likely be productive. There would seem to be no reasonable doubt that such mid-interval pain is linked up with the occurrence of ovulation, although the exact mechanism is not known, nor the precise chronological relation with the discharge of the ovum from the follicle. Fortunately, mittelschmerz of sufficiently severe intensity to inhibit coitus is rare, but unfortunately the minor degrees of ovulation pain are also comparatively infrequent. When they do occur the patient flies a flag, so to speak, to indicate the approximately optimum phase of her cycle from the standpoint of fertilization.

It is fortunate that Krohn included a study of basal temperatures, since there is still doubt as to the exact time relation of the characteristic rise in ovulatory cycles to ovulation itself, though there is little doubt that the postovulatory rise is due to the progesterone produced after ovulation. The results reported by Krohn confirm the uncertainty as to the time relationship between actual ovulation, basal temperature elevation and the occasional subjective ovulation pain.

My own feeling is that the temperature rise need not be interpreted as a sudden call to arms or a fire alarm, or as an indication that the husband be telephoned for to come home at once and do his duty. It means simply that ovulation has occurred at about the time of temperature rise, or a little before or after.

I am afraid that I have often incurred the wrath of my good friends among the basal temperature enthusiasts by maintaining that in ovulating women with an approximately nor-

continued ignorance of the mechanism of this common disorder, as to the validity of the distinction which he draws, and of the reliability of the simple clinical methods which he describes for the differentiation of the two types.

Any discussion of the point will probably have to be theoretical as far as most of us are concerned, since I suspect that few have made any effort at such clinical tests as he describes. However, one may be forgiven considerable skepticism in accepting the causative role of sclerocystic ovarian changes in ovarian dysmenorrhea especially since the ovaries of dysmenorrhea cases are the very ones in which a normal functioning activity, certainly as regards ovulation, may be more or less presupposed. Again, the studies which Browne reports on nerve changes which he interprets as degenerations of the peri- and intra-fascicular ovarian nerves, will need confirmation before they can be generally accepted. On such still doubtful points his technic of severance of the ovarian nerves by ligating the infundibulopelvic ligaments, and incidentally the ovarian vessels, is based, with the possibility of ovarian circulatory disturbance.

If there are really two separate and distinct types of primary dysmenorrhea, and perhaps there are, the uterine variety must certainly be much the more common, if one may judge from the high incidence of relief, varying from 60 to 90 per cent, from presacral neurectomy, reported in the innumerable papers on the subject. As a matter of fact, so good are the results that I fear the operation is resorted to by a good many gynecologists on very slight provocation, and probably is often imperfectly executed. The operation is not a difficult one, but it is not altogether without hazard, even deaths having been reported. My own feeling has always been that it should be reserved for the severe cases in which the patients can not be kept reasonably comfortable by non-surgical measures. In my own practice I do more neurectomies as secondary procedures in combination with operations directed primarily at other indications, than I do for dysmenorrhea per se. For example, in operations for endometriosis one can not be sure that the conservative procedure most often employed will relieve the severe dysmenorrhea of which the patient complained, and the extra-added procedure of presacral neurectomy is often wise.

I note that Browne believes that primary dysmenorrhea may be the result of prolonged celibacy, a statement hard to reconcile with the fact that the great majority of cases date from the menarche or within a year or two of the latter. In others the dysmenorrhea appears when ovulation is inaugurated. With Joe Meigs urging a similar factor in endometriosis and preaching early marriage and childbearing, it looks as if the fathers of the nation will bear a heavy burden if they enlist in an anti-dysmenorrhea and anti-endometriosis campaign for the benefit of their very young married daughters.—Ed.)

INTERMENSTRUAL PAIN (THE "MITTELSCHMERZ") AND THE TIME OF OVULATION

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Brit. M. J., 1: 803, 1949

Cyclically recurring pain in the pelvis which can be related to the phases of the menstrual cycle, is not uncommon in women. The periodicity of intermenstrual pelvic pain is one of the many signs that have been taken to indicate the time of ovulation.

The author reports a case of a married woman, 28 years old, in whom cyclical intermenstrual pain has been recorded without interruption for $4\frac{1}{2}$ years. The

chance of success are those in whom the period of amenorrhea, prior to irradiation, has not lasted more than 30 months. The treatment proved successful in 76% of cases in whom amenorrhea had existed from 4 to 12 months. The rate of success depends upon the degree of development of the genital tract. The most successful were those in whom the length from the external os to the fundus uteri was at least $1\frac{1}{2}$ inches. This measurement was adopted in attempting to estimate the degree of hypoplasia in the uterine body and cervix.

The ages in this series varied between 17 and 31. It does not appear that, between these ages, the age plays much part in determining the chances of success. It is not advisable to attempt this form of treatment for secondary amenorrhea in those under 16 or over 40 years of age.

It is essential that every woman should have a thorough clinical examination prior to irradiation, and no one treated in whom any clinical disease can be demonstrated. All possibility of pregnancy should be excluded.

(Numerous reports as to the frequent effectiveness of low dosage irradiation of the pituitary and ovary in the treatment of amenorrhea have appeared, and the method is employed by a good many excellent gynecologists. On the other hand, as I have previously discussed in these pages, there is a large block of gynecologists who seldom or never employ the method. Their reluctance to do so is not based upon any fear of permanent injury to the pituitary or ovaries, because, as the authors of the above paper state, there is little or no evidence to justify this fear. Nor does there appear to be any great risk of injury to the immediate offspring in those cases in which pregnancy later occurs, if one may judge from the comparatively small number of reports on cases of this sort.

The reluctance of many of us in resorting to this plan of treatment very frequently is based largely on the warnings of geneticists as to damage which might be inflicted not on the second, but on the third and later generations of offspring. Some of our readers will recall the impressive presentation of Clarence Little, one of our leading geneticists, at a meeting of the Section of Obstetrics and Gynecology of the American Medical Association some years ago. The studies which he made on experimental animals seemed to leave no doubt as to the deleterious effects of even very low dose irradiation upon these later generations. Similar observations have been made by other geneticists, who believe that damage is often inflicted upon the genes by even very low X-ray dosage.

Whether these observations can be expended to the human one can not be absolutely sure, but it seems highly probable on general biological grounds. The simple fact is that as yet there are no reports available as to possible damage inflicted upon grandchildren of women who have been treated by the plan under discussion. In any event it is this long range consideration which makes cowards of many of us in the application of this method of treatment. We have come to realize, especially in the treatment of cancer, that irradiation is not an unmixed blessing in gynecological therapy, and that at times it does more harm than good. And this may apply to even very low, presumably harmless dosage. Only recently our newspapers have been full of the possible hazards to shoe-store customers and salesmen from the simple shoe-fitting X-ray devices so widely employed, and these warnings come from competent radiologists.

So far as I can see, each gynecologist must decide for himself on the basis of the still very incomplete evidence pro and con whether or how often he will employ this plan of treatment. In resolving this question he should remember that amenorrhea in itself is a perfectly harmless disorder, that in certain cases it needs no treatment at all except reassurance, in others simple constitutional measures only, while in still another group simple endocrine therapy of one sort or another must be added. It is the commonly associated sterility which is the chief justification for treatment in most cases, and everyone appreciates the weight, as well as the frequency of this indication.

mal and regular cycle length, it may be assumed that ovulation will occur almost always at the established ovulation span, which embraces a few days before and after the 14th day preceding the next menstrual date. All the histological and basal temperature studies which have ever been made have confirmed this belief, although there are no doubt some individual exceptions. My own custom with such women, whether right or wrong, is to advise that they go easy with coitus at other times, but that they concentrate on the favorable period with frequent coitus, at least once every 48 hours. It seems to an old fashioned fellow like myself that such a simple plan as this is about as likely to be successful as if the supplementary use of a basal temperature curve were invoked. Certainly there can be no criticism of the latter, my own point being that in women of the type under discussion basal temperature studies are far less important than in their employment as a simple ovulation test, or their value in women of very irregular cycle lengths, in whom it is impossible to predict the optimum or ovulation span even approximately.—Ed.)

TREATMENT OF SECONDARY AMENORRHEA WITH LOW DOSAGE IRRADIATION OF OVARIES AND PITUITARY GLAND

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J. Obst. & Gynec. Brit. Emp., 56: 260, 1949

The authors report 21 cases of secondary amenorrhea treated with low dosage irradiation of the ovaries and pituitary gland. They define a case of secondary amenorrhea as one in whom a period has occurred, but in whom there has been at least 4 months of amenorrhea.

From a review of the literature, it seems safe to assume that low dosage x-rays have never been proved, on cytological grounds, to damage either the pituitary gland or the ovaries permanently, provided the x-rays are properly applied. The variation between a harmful and a safe dose is probably small, and anything other than small variations in dosage should be avoided. In each case high voltage therapy was used, consisting of 200 kV. at 15 m.a. with a filtration of 1.5 mm. of copper and 1 mm. of aluminum. The focal skin distance for each field was 50 cm. The ovaries were treated by right and left anterior and posterior fields, using 15 x 15 cm. applicators. The pituitary was treated by a central field on the forehead, aimed at the sella turcica, sized 6 x 8 cm. On the first day, 75r were given to right and left anterior pelvic fields; 75r given to the pituitary field. On the 7th day, 75r were given to right and left posterior pelvic fields. On the 14th day, the same procedure as that on the first day was carried out.

A case was considered to be successful if, within 6 weeks of irradiation, a menstrual cycle of from 21 to 40 days was established. If the periodicity was more than 40 days, but still fairly regular, the case was considered improved. If there was no alteration, it was considered to be a failure. In 14, or 66.6%, a normal periodicity was produced; in 2, or 9.5%, the periodicity was improved, and in 5, or 23.9%, the treatment failed.

It appears that the cases of secondary amenorrhea in whom there is the greatest

VULVA AND VAGINA

ROENTGENOGRAPHY OF VAGINAL CYSTS

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J. Obst. & Gynaec. Brit. Emp., 56: 228, 1949

The author presents 3 cases of vaginal cysts correctly diagnosed by x-ray. Case I had a protrusion in the perineal region which most closely resembled a rectocele, but palpation left open the possibility that a tumor was lying between the descended posterior wall of the vagina and the rectum. X-ray examination with opaque medium showed that the protrusion was an independent cystic neoplasm associated with a rectocele. In Case II, it was not possible by routine examination to decide whether a prolapse of the posterior vaginal wall alone was present. X-ray examination with contrast substance proved that beside the rectocele there was a coincidental cystic tumor. Case III had a tense swelling in the right gluteal region. The nature of this growth could be ascertained only by means of x-rays which revealed clearly an air-containing and well-outlined cyst having no communication with adjacent organs.

These cases illustrate that radiographic evidence may be of great value in cases in which the possibility of a vaginal cyst arises and the routine methods leave the diagnosis undecided.

(Although the x-ray procedure recommended by the author may in rare cases be helpful, I cannot believe that there are many cases in which simple vaginal and rectal palpatory methods will not suffice to detect the presence of vaginal cysts. In his case III, the nature of the tense swelling in the gluteal region could probably have been more simply settled by aspiration.—Ed.)

A FALSE VAGINA FORMED BY COITUS

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J. Obst. & Gynaec. Brit. Emp., 56: 269, 1949

The patient was a 35 year old woman admitted with complaint of lower abdominal pain and swelling of 10 months' duration. Ten years previously, she had been delivered of a large stillborn infant. Pelvic examination revealed the introitus to be stenosed, admitting only a probe. Between the fourchet and the anus was a depression 2 inches deep. The patient stated that since her illness

This is not the place for a full discussion of the treatment of amenorrhea, but my own feeling is that one should not resort to any such rather drastic plan as irradiation except in the long standing and intractable cases. I have probably gone to an extreme in this respect, which probably explains why my own results in the small group in which X-ray has been used have been so much less favorable than those reported by others in milder cases, with sometimes amenorrhea of only a few months duration. Just to be perverse, I feel that in many of these menstruation would have been reestablished either spontaneously or with very simple plans of management, even though X-ray treatment had not been employed.—Ed.)

TREATMENT OF MENOPAUSE BY ESTRADIOL PELLET IMPLANTATION

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New York State J. M., 49: 1175, 1949

From the endocrine standpoint, the menopause may be considered to be a condition of deficiency of the ovaries. Conventional hormone therapy has been substitution therapy with estrogens in an attempt to compensate for the diminishing ovarian folliculoid production until the pituitary becomes adjusted to the diminished level of activity of the entire endocrine system.

The present study is concerned with 11 cases of severe menopause in which the usual parenteral and oral estrogen therapy, sedatives, hypnotics, and psychotherapy had been ineffective. In 10 of these patients, one 25 mg. estradiol pellet was implanted subfascially into the lateral aspect of the thigh. One patient received an additional 25 mg. pellet 6 months after the first implantation. In all cases, estradiol pellet implantation therapy brought prompt relief of all symptoms for periods of 6 to 11 months. Estradiol pellet implantation most nearly approaches ideal estrogen therapy. It most nearly approximates physiologic, endogenous estrogen production.

(On a good many previous occasions I have in these pages expressed my own feeling with reference to estrogen pellet implantation in the treatment of menopausal symptoms. I have never been able to engender the slightest enthusiasm for it, and I believe it to be both unnecessary and unwise. Those who employ it emphasize that it keeps up a steady supply of estrogen, but this to my mind, is its chief disadvantage. Contrary to the author, I do not believe it is physiologic, because normally and physiologically the estrogen should be disappearing at the time when menopausal symptoms sometimes call for treatment. The purpose of estrogen therapy is not to restore the premenopausal hormonal status, but simply to ease the patient over the symptomatic bumps which may occur, usually periodically, during the period of readjustment. The effective modern oral preparations permit of far greater flexibility in treatment. The estrogen is given only when and if the vasomotor symptoms are sufficiently troublesome, and certainly not constantly. Such constant estrogen administration may, aside from other such hazards as bleeding, actually prolong the menopause by keeping up a vicarious or substitutal ovarian function, thus delaying the pituitary-ovarian readjustment which is inevitable at this epoch.—Ed.)

(In view of the relative frequency of amebic dysentery, and the frequency with which the vagina is invaded by other parasites, it is strange that amebic vaginitis has not been more often observed. The genuinely amebic character of the vaginitis in this case is well supported by the finding of the parasite in the vaginal discharge and the prompt response of the infection to emetine therapy.—Ed.)

BACTERIOLOGY OF THE VAGINA IN 75 NORMAL YOUNG ADULTS

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Surg., Gynec. & Obst., 87: 410, 1948

Unmarried student nurses ranging from 17 to 25 years of age were studied with vaginal cultures and smears. A glass cylinder was introduced into the vagina and a cotton swab contained in the cylinder was then pushed from its protected position and carried 2–4 cm. higher. After the swab had been twirled a few times, it was withdrawn into the tube and the tube withdrawn. The pH of the vagina was then determined. Cultures were planted aerobically, anaerobically, under increased carbon dioxide tension, and on Sabouraud's medium. Colonies which appeared to belong to the coliform group were sub-cultured to desoxychillate plates and carbohydrate fermentation tubes.

Lactobacilli were cultured from 82.6% of the subjects; and stained smears furnished presumptive evidence that lactobacilli were present in 100% of the cases. In 49.3% of the subjects Doederlein's bacilli only were found. In 33.3%, Doederlein's bacilli and other organisms were present; and in 4%, organisms other than Doederlein's bacilli were present. In 13.3% of the subjects, the cultures were sterile. If Doederlein's bacilli only are present, the vaginal pH is always 4.5. If other complexes are present, no correlation with the pH can be demonstrated. Besides lactobacilli, other organisms obtained by culture were: diptheroids, staphylococcus albus, streptococci, coliform organisms, and yeast-like fungi. All of the streptococci were adapted to a low oxygen environment. No culture was positive for streptococcus fecalis. Coliform organisms were discovered in only one instance.

Four individuals harbored *Candida stellatoidea* and *Candida Krusei*. Although these yeasts are believed to be causes of vulvo-vaginitis, the individuals from whom they were obtained had no pruritus.

(Perhaps the most interesting result of this painstaking bacteriological study is the demonstration of the constancy of a vaginal pH of 4.5 if only Doederlein bacilli are present, and the lack of any correlation with the vaginal pH in the presence of other bacteriological complexes.—Ed.)

coitus had taken place at this site. A large nodular mass was palpable abdominally and rectally, and was diagnosed as a fibromyomatous uterus. At operation the fallopian tubes were found to be occluded at their fimbrial ends. Myomectomy and salpingostomy were performed. The vagina was dilated after radial incisions had been made. The vaginal vault was found to be normal, although the left fornix had been obliterated. A large glass vaginal dilator was left in situ. The patient was sent home with instructions to wear the glass dilator for 6 months, removing it only for douching, menstruation and intercourse.

(In lieu of any inspired scientific comment upon this particular husband's deviation from the true marital path, and to lighten the profundity of the editorial contribution, I wonder if I might relate another Rabelaisian story of the type which has occasionally befouled these pages. It has to do with a traveling salesman—now you know what is coming and can stop here if you like—who, during a visit to an Indian reservation village, lured a not unwilling squaw into the woods. During their little act of devotion, the squaw kept exclaiming, "Oolah! Oolah!". He had no idea what she meant, and was still wondering about it when later in the evening he visited a billiard parlor, where a number of Indian bucks were playing the game. Every now and then one would utter the same mystic word, "Oolah". On inquiring of one who spoke English, he was told that the word meant "wrong hole." Could this have been another case of the type reported by the author of the above paper?—Ed.)

AMOEBIC VAGINITIS

N. C. SEN

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Brit. M. J., 1: 808, 1949

The author reports a case of amebic vaginitis. The patient was a 35 year old Nepalese woman complaining of profuse seropurulent vaginal discharge and swelling and pain in the perineum following a severe attack of dysentery. Pelvic examination was done under general anesthesia. There were linear ulcers in the vagina; these ulcers were superficial, with a punched-out appearance. The cervix was slightly enlarged, soft, and ulcerated. Examination of the vaginal discharge revealed many active forms of *E. histolytica*. Scrapings from the ulcers revealed active *E. histolytica*. Examination of the stools revealed cysts of *E. histolytica*, but proctoscopy showed no ulcer in the lower anorectal canal. After 12 gm. of emetine in 15 days, the ulcers were completely healed and the patient felt perfectly well.

Three points favor the diagnosis of amebic vaginitis: (1) vegetative forms of *E. histolytica* in the discharges, (2) rapid cure with specific amebicidal drugs, and (3) the punched-out appearance of the ulcers. Infection of the vagina is presumably by continuity and contiguity with the anorectal canal. The cervix is involved in about 70% of the reported cases.

Following radium application, the immediate picture is that of irritation; atrophy does not set in until a few months later. The walls become rigid and close in from all sides. Cases of coalescence before the atrophic picture is complete have been observed.

Atrophy of the vaginal mucosa may not cause any symptoms unless predisposing factors to infection are present. Such factors include coitus, lowered bactericidal power, and constant friction between the approximated surfaces.

Coalescence usually begins slightly below the mid-part of the vagina. In about 6 weeks' time, the block is complete.

For the severe cases in the postpartal group, the authors used a polyglandular extract which contained a bit of everything, according to the labels. The mixture was of unknown potency and was given intramuscularly every other day in 10 cc. doses. This was supplemented with rather heavy doses of thyroid and estrogens. Moderate improvement in general and local symptoms was obtained. The premenopausal group was very successfully treated with estrogens. The latter were used with caution and with regard for their carcinogenic potentialities. Estrogen therapy gave questionable results in the postmenopausal group. The vitamins were not employed in therapeutics.

Lowered blood estrogen levels probably are the major cause of vaginal atrophy. Postpartum pituitary damage may contribute to the condition. Local infection probably plays an important role in the premenopausal group.

(There is no doubt that the vaginal mucosa, like that of the uterus and tubes, and the mammary glands as well, shows varying degrees of sensitivity or refractoriness to the ovarian hormones. The fact remains, however, that atrophy of the vaginal mucosa rarely produces clinical problems unless the ovarian function is completely withdrawn, either permanently or sometimes only temporarily, for perhaps a long period of time. The latter, for example, might be the condition in the relatively rare group of the authors' "postpartal" (postpartum would seem to be a better word) cases, in which the long-standing amenorrhea is due to temporary cessation of ovarian function. The permanent abolition of ovarian function after the natural or artificial menopause, whether the latter be due to surgery or radiation, is easy to understand, and it is this group which every gynecologist has frequent occasion to treat.)

Not many will wish to emulate the authors by giving the post-partum cases a "glandular extract containing a bit of everything." Nor is it rational to treat premenopausal patients, who are presumably still menstruating normally and whose own ovaries are probably still producing ample estrogen, by administration of estrogens. It is the senile atrophy and senile vaginitis which so often develop after the menopause which often constitute a troublesome clinical problem. It is rather surprising to note that in this group the authors' results were poor, while the treatment of the premenopausal group was very successful.

In the postmenopausal or senile group estrogen therapy is often helpful, especially when carried out by means of the vaginal suppository method. But the good results are temporary, so that frequent but interrupted courses of the treatment are necessary. Moreover, in the severe grades of atrophy, with shrinkage of the entire vaginal canal, colpoplastic procedures are often necessary. In the case of the multiparous woman who arrives at the menopause with a widely patulous canal, even a considerable degree of atrophy may entail no coital difficulty, and, indeed, it may at times even add to the woman's coital charms. On the other hand, the nulliparous woman with a rather small vaginal orifice may encounter difficulty if the canal undergoes marked senile shrinkage.—Ed.)

ATROPHY OF THE VAGINAL MUCOSA

A Clinical Study of Thirty-eight Cases

J. C. YIN, T. H. LIU, AND M. L. YIN

Dept. of Obstetrics and Gynecology, College of Medicine, National Central University, Nanking, China

J. Internat. Coll. Surgeons, 12: 357, 1949

Atrophy of the vaginal mucosa almost always results from ovarian deficiency; atrophic changes may take place during any period of a woman's life.

Over a 6 year period, 38 patients with atrophic changes of the vaginal mucosa were observed and followed from 3 to 5 years. Atrophy of the vaginal mucosa can be divided into 4 groups: (1) postpartal, (2) premenopausal, (3) postmenopausal, and (4) artificial, surgery and irradiation. The earliest sign of atrophy of the vaginal mucosa is a smooth, pale appearance of the whole canal. This is followed by the appearance of telangiectatic spots, first over the portio vaginalis of the cervix, then the upper part of the vagina. These spots are found more frequently in the premenopausal and senile groups. Schiller's test may show patches in the cervix and upper vagina which fail to take up the stain. The epithelium over the telangiectatic spots takes up the stain. Later, the vaginal canal gradually narrows, with increasing rigidity of the walls. Thickening takes place mainly in the submucosa.

In the postpartal group, the whole genital tract appears atrophic and the uterus is either super- or hyperinvolved. The vaginal canal is narrow; telangiectatic spots over the mucosa are not common. In the mild forms, the patients show little or no sign of endocrine disturbance other than amenorrhea. The vaginal canal narrows down very gradually and rigidity is not marked. The atrophied mucosa is constantly exposed to trauma from coitus and friction of the walls of the vagina against each other; coalescence may often be the end result.

The typical history of the postpartal group is of prolonged and continuous amenorrhea for years after a childbirth. The labor may or may not have been difficult, but the patient had either suffered from excessive blood loss or the puerperium was febrile and stormy. Neglected cases of dystocia may result in marked atrophy of the vaginal mucosa. This type of atrophy rarely lasts more than eight months.

In the premenopausal group, most of the patients had passed their 40th year. The vaginal canal is neither rigid nor narrow. Telangiectatic spots are located mainly over the cervix and upper vagina. The patients usually come in with a bloody vaginal discharge and the clinical picture is that of slight atrophy plus some mild infection.

In the senile group, the vaginal canal is narrow and shrunken, the mucosa may be smooth and shiny. Linear cracks or red streaks may appear in the vaginal canal, but they do not have the same appearance as the telangiectatic spots found in the premenopausal group.

CHLOROMYCETIN IN THE THERAPY OF GRANULOMA
INGUINALEROBERT B. GREENBLATT, VIRGENE S. WAMMOCK, ROBERT B. DIENST,
AND ROBERT M. WEST*University of Georgia School of Medicine, Augusta, Georgia*

J. M. A. Georgia, 38: 206, 1949

Granuloma inguinale has been experimentally treated with all the new antibiotics. The disease is resistant to penicillin; it may be very effectively treated by streptomycin (20 gm. in 5 days); aureomycin (20 gm. over a 5-10 day period) has also been very effective. Streptomycin and aureomycin both have the disadvantage of requiring hospitalization.

Chloromycetin is supplied in capsules containing 250 mg. each, for oral administration. Five cases of granuloma inguinale were treated with chloromycetin, using 20 gm. in a period of 5 to 10 days. The therapeutic results were spectacular. No toxic effects were observed.

It is emphasized that this is only a preliminary report.

(The studies which are being made on the treatment of both granuloma inguinale and lymphogranuloma inguinale with the antibiotics are still too new to evaluate with any precision, but the generally good results being reported would seem to justify the hope that this will be the method of choice from now on. Thus far streptomycin appears to be yielding the best results, if one may judge from such reports as those of Stewart and Laur, and Jacoby and his associates, as abstracted in the present issue. The results with chloromycetin in the small group of 5 cases reported by Greenblatt and his associates seem equally good, but we shall have to wait, but probably not very long, to evaluate this new niche for the employment of the antibiotics.—Ed.)

AMBULATORY TREATMENT OF GRANULOMA INGUINALE
WITH STREPTOMYCIN

ADOLPH JACOBY, THEODORE ROSENTHAL, AND NATHAN SOBEL

Social Hygiene Clinics, Dept. of Health, City of New York, N. Y.

Am. J. Syph., 33: 76, 1949

A total of 37 patients were treated in the outpatient clinic with intramuscular injections of streptomycin in either an oil-beeswax mixture or an aqueous solution on each of 7 to 12 consecutive days. The majority of the patients received intramuscular injections of 3 gm. daily. The total dosage administered varied between 10.5 and 51 gm. in a period of from 6 to 29 days.

Of the 4 patients receiving beeswax and oil, 3 were cured after having received from 15 to 20.4 gm. of streptomycin in a period of from 13 to 52 days. Two of these patients remained well after periods of 3 and 4 months; the other, having

THE MANAGEMENT OF THE RIGID HYMEN AND PERINEUM
EARLY IN MARRIAGE

WALTER J. REICH AND MITCHELL J. NECHTOW

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J. Internat. Coll. Surgeons, 12: 364, 1949

The rigid hymen is frequently encountered at a routine pre-marital examination. The patient is instructed to attempt natural intercourse. If she is unsuccessful, she returns for further management.

The psychosomatic status of the patient is evaluated and psychiatric therapy is undertaken if necessary. Surgically, the best approach is a complete circular hymenectomy. This procedure is followed by a mid-line perineotomy. The longitudinal incision is closed transversely. One week postoperatively, vaginal dilations, using the authors' special dilator, are begun and continued twice weekly for one month.

(There is no doubt that the early days of married life may have much and sometimes lasting influence on the later attitude and sex responses of the wife. The honeymoon is not always a brilliant success from a sex standpoint, and the frequent difficulty in sex adjustment may have serious psychosomatic repercussions in the later sex life of the couple. This is too big a subject to enter upon here, and the only point I wish to emphasize is that such actual mechanical factors as an unusually rigid hymen are very soon complicated by the psychic factor. Pain is always an accompaniment of attempted coitus in the presence of mechanical obstacles, so that the woman soon dreads the approach of the husband and the factor of psychogenic vaginismus is added to the purely mechanical one.

The rigid hymen is more often encountered in the older group of patients, though there are exceptions. The circular hymenectomy recommended by the authors is practised by many gynecologists, but it has the disadvantage of leaving an annular and sometimes painful cicatrix. In most cases I prefer a wide divulsion of the orifice under anesthesia. This usually produces multiple radial lacerations of the hymen, simulating the effects of complete coitus, and occasionally requiring hemostasis. It leaves the orifice surrounded by a fringe of carunculae myrtiformes just as does complete coitus, and less sensitive than the annular scar of circular hymenectomy. Reassuring and instructional talks are usually necessary to ensure good results.—Ed.)

CHLOROMYCETIN IN THE THERAPY OF GRANULOMA
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Of the 4 patients receiving beeswax and oil, 3 were cured after having received from 15 to 20.4 gm. of streptomycin in a period of from 13 to 52 days. Two of these patients remained well after periods of 3 and 4 months; the other, having

received 20.4 gm. of streptomycin, relapsed after one month's time. The 4th patient was definitely not healed. Of the 33 patients receiving aqueous injections, 30 were healed in a period varying from 9 to 59 days. Twenty-seven of these remained healed for from one to 5 months. Of the original 37 patients, 32 were eventually cured, 2 are still uncured, one is still under treatment, and 2 failed to return for observation.

The duration of the disease may have some bearing on the results obtained. Approximately 90% of those having the disease from one to 12 months, were cured; whereas, 4 of the 6, or 67% of those having the disease from one to 10 years, were cured. The presence or absence of previous medication does not seem to have any influence on the effect of streptomycin.

Most of the patients reported diminution of pain and discomfort in the lesions within 24 hours after the beginning of therapy. Healing of the lesion began within one week after initiation of therapy.

(See comment on following abstract of paper by Stewart and Laur.—Ed.)

STREPTOMYCIN THERAPY OF GRANULOMA INGUINALE

JOHN J. STEWART AND WILLIAM E. LAUR

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Am. J. Syph., 33: 65, 1949

The authors report 15 cases of granuloma inguinale treated with streptomycin. All of the patients were negroes, aged 23 to 43. There were 9 men and six women. In 10 patients, the lesions had been present for more than 6 months, and in 5, for less than 6 months. Thirteen patients received 20 gm. of streptomycin in 11 days as follows: 3 gm. daily, in divided doses at 4-hour intervals, for 3 days; 2 gm. daily in divided doses at 4-hour intervals for 3 days; 1 gm. daily, in divided doses at 4-hour intervals for 5 days. Of the 2 remaining patients, one was given 1 gm. streptomycin daily, in divided doses at 4-hour intervals for 15 days, and the other received 4 gm. daily, in divided doses at 4-hour intervals, for 5 days.

All patients felt subjective improvement within 24 to 48 hours and all showed complete or nearly complete healing in 10 days to 3 weeks. Five patients have been followed 4 months or longer. In none of the entire group has relapse been observed.

(Already it seems quite clear that the antibiotics are going to revolutionize the hitherto not so successful treatment of both granuloma inguinale and lymphogranuloma inguinale, and, from the comparatively few reports thus far available, it would seem that streptomycin, aureomycin and possibly chloromycetin offer more hope than penicillin. If the extremely striking benefits reported by the above authors and a few others from the use of streptomycin in granuloma inguinale are maintained through further observations and reports it would seem that this disease should be a readily controllable one.—Ed.)

THE UTERUS

RUPTURED PYOMETRA AS A SURGICAL EMERGENCY

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J. Obst. & Gynaec. Brit. Emp., 56: 237, 1949

The patient was a 72 year old woman complaining of acute abdominal pain for one day. Five years previously the patient had had a repair of genital prolapse. Since then she had had a vaginal discharge. On examination there was slight distension and generalized rigidity of the anterior abdominal wall with tenderness all over. No masses were felt in the abdomen. On rectal examination extreme tenderness was present in the pouch of Douglas. No mass was felt in the pelvis. A tentative diagnosis of perforation of a carcinomatous viscus was made. At laparotomy, a large quantity of thin greenish pus was present throughout the peritoneal cavity. A small perforation was seen on the anterior surface of the uterus just below the fundus. Hysterectomy with bilateral salpingo-oophorectomy was performed. A midline suprapubic tube drain was inserted down to the pouch of Douglas and the incision closed. A piece of omentum protruded from the center of the wound, but 36 days after operation the patient was discharged.

Pathologic examination showed the wall of the uterus to be thin and markedly distended. Section showed complete absence of endometrial tissue, which had been replaced by a pus and round cell response. The general appearances were those of pyometra with no evidence of malignancy.

There seem to be very few references in the literature to rupture of the uterus other than that due to causes connected with pregnancy. The case presented here would seem to be due to operative interference with the cervix in the course of a plastic vaginal repair with senile atresia as an alternative or contributory cause.

(Pyometra itself is not extremely rare, being due most often to malignancy, senile cervical atresia, or to radiotherapy. Rupture of a pus-distended uterus, however, must be extremely rare, and no such case has come under my own observation. I would be inclined to believe that the senile factor was perhaps more important in the production of the pyometra in the reported case than the one of previous operation.—Ed.)

FIBROADENOMA OF THE CERVIX WITH ADENOMYOSIS
OF THE UTERINE BODY

J. PRESTON MAXWELL AND J. P. S. WHITEHEAD

White Lodge Hospital, Newmarket, England

J. Obst. & Gynaec. Brit. Emp., 56: 246, 1949

The patient was a 33 year old unmarried, mentally defective woman with a grape-like growth filling the vagina. The mass distended the vagina and was approximately the size of a small orange. Sections showed no definite abnormality except for the evidence of chronic cervicitis. Panhysterectomy was performed. There was no sign of invasion of the broad ligaments. The patient made a rapid recovery and there was no sign of metastasis or recurrence. Additional slides were examined. Uterine glands deep in the muscle tissue were suggestive of adenomyosis. The glands in the cervix showed a polypoid growth. Prof. James Young examined the sections and is of the opinion that there is adenomyosis of the uterine body and that the cervical growth is a fibroadenoma.

(The senior author of this paper spent many years of his earlier life in medical work in China and one of his sabbatical years was devoted to work at the Johns Hopkins Hospital, where he made many friends. We send him salutations across the seas and are glad that in his sunset years his enthusiasm and his professional interests appear to be undiminished.

The interesting case which is abstracted above can in a broad sense be spoken of as a fibroadenoma, but an examination of the photomicrograph which accompanies this paper convinces me that the glands described deep in the cervix are of Wolffian or Gartner duct origin. This vestigial structure courses through the broad ligament close to the lateral wall of the corpus and cervix, but occasionally it is found in the musculature itself. In the cervix it may develop a markedly adenomatous tendency and at times may even give rise to an adenocarcinoma, though this is rare. The Wolffian tubules may penetrate deeply into the cervical stroma, but they can usually be easily distinguished from the characteristic cervical glands by the character of the epithelium and the tubular pattern of the gland-like structures. I have encountered a number of instances of this lesion and scattered observations of this sort have been reported by various authors over the years. Meyer described the condition fully and called attention to the occasional occurrence of similar vestigial adenomata in the lateral vaginal fornices, occasionally producing ulcer-like lesions which may easily be mistaken for carcinoma. The most recent publication on the subject, and it is an excellent one, is that of Huffman (Am. J. Obst. & Gynec., 56: 23, 1948).—Ed.)

TUBERCULOSIS OF THE ENDOMETRIUM TREATED WITH
STREPTOMYCIN

Report of a Case

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West. J. Surg., 57: 243, 1949

Numerous cases of unsuspected endometrial tuberculosis have been brought to light by routine biopsy and curettage in women complaining of infertility and menstrual irregularities. In many of these cases, no lesion has been demonstrable outside of the genitalia. The use of streptomycin in pelvic tuberculosis has not been reported before.

A 28 year old housewife complained of sterility and irregular menses. There was a family history of pulmonary tuberculosis. Endometrial biopsy showed a granuloma typical of tuberculosis. There was no evidence of tuberculosis elsewhere in the body. Tubercle bacilli were cultured from the endometrium.

The patient was treated with streptomycin 1.0 gram daily for 58 days. Histopathologic and bacteriologic studies showed no evidence of tuberculosis in the endometrium over a period of 6 months following treatment. A menstrual irregularity of 2 years' duration was simultaneously corrected.

(The striking results of streptomycin in at least certain cases of tuberculosis would seem to justify its trial in a case of the type described in this abstract. The condition treated, however, is probably not one of simple endometrial tuberculosis, since the latter is nearly always secondary to tuberculosis of the tubes. From time to time endometrial biopsy done in the investigation of sterility reveals unexpected tubercles of the endometrium, and some foreign investigators, especially Sharman of Edinburgh and Schockert of Louvain, have reported the rather startling incidence of 5 per cent for cases of this type. This is considerably higher than has been noted by most of us, and I have thought that it might be due to the fact that only one or 2 sections are routinely made of the endometrial tissue. Perhaps we too might find tubercles more often if a larger number of sections were made at different levels in the block.)

When unsuspected endometrial tuberculosis is thus revealed, one often finds no symptomatic or palpatory evidence of adnexal involvement, and the tendency of most of us is to treat such cases expectantly and constitutionally. In my own experience, evidences of the tubal involvement usually appear sooner or later, and surgical treatment has been indicated. Always, in my own experience at least, tuberculosis has been demonstrable in the tubes. But during the waiting period streptomycin might well be employed, as in Schaupp's case, although it is probably too early to know, since only 6 months have elapsed, how much or how permanent the effect of the treatment has been upon the endometrial and the probably associated tubal tuberculosis. We shall have to wait for more and longer observations before any conclusions are drawn.—Ed.)

CARCINOMA OF THE UTERINE CERVIX; THERAPEUTIC PROBLEM

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Ann. West. Med. & Surg., 3: 126, 1949

This study is inspired by the recent revival of interest in the surgical therapy of cervical carcinoma. The author studied 66 cases of carcinoma of the cervix. On admission 15.5% of the patients were in stage I, 55% in stage II, 24.5% in stage III, and 5% in stage IV.

The patients in this series were usually given x-ray therapy prior to radium therapy. No trans-vaginal x-radiation was employed. Radium therapy was individualized within the conventional limits.

Four of the patients had serious sequelae. One patient had an extensive proctitis, one a recto-vaginal fistula, and 2 had bullous edema of the bladder.

In stage I, the 5-year cure rate was 89%; in stage II, 72%; in stage III, 9%; in stage IV, 0. In stages I and II combined, the net 5-year cure rate was 74%.

It is difficult to do a complete operation for cancer of the cervix and maintain the integrity of the bladder and ureters. On the other hand, irradiation produces a cancericidal dosage in the supracervical area, the very place where surgery is most hazardous.

The author feels that there is no reason for abandoning irradiation as the primary method of treatment for squamous carcinoma of the cervix. The most promising future development is the selection of radio-resistant lesions for radical surgical procedures after a trial with irradiation.

(While the series reported is a small one, the results reported in the Stage 1 and Stage 2 cases are surprisingly good, in spite of the inevitable bugbear of possible radiological visceral injury, as illustrated by the 4 serious sequelae reported in this group. I do not believe that the results in this particular group would have been equalled if surgery had been employed in any considerable proportion of the cases. I emphasize this because I feel very strongly that in the present fluid state of the problem of cervical cancer therapy, radiotherapy should be the favored plan in the smaller clinics, leaving the radical surgical plan to the larger clinics with the very full facilities required for this, especially in the form of surgeons who are expert in the performance of the often difficult and formidable surgical procedures which may be called for. Unless thus equipped, the best results, with the least mortality and morbidity, will accrue from sticking to the radiotherapeutic plan, especially if radiologists continue their efforts to develop technics designed to lessen the incidence of unfortunate radiological sequelae.—Ed.)

CARCINOMA CORPORIS UTERI IN ONE HORN OF A UTERUS BICORNUIS UNICOLLIS

R. M. CORBETT

Preston, Ireland

Irish J. M. Sc., 281: 231, 1949

The association of a bicornuate uterus with carcinoma is a definite rarity. The author reports the case of a 54 year old woman, 8 years past the menopause, who had had slight bleeding for 18 months. At laparotomy, the uterus was bicornuate and the horns were widely separated. Histologically, adenocarcinoma was present in the left horn but not in the right. The left horn showed 2 small myomata.

The author points out that a negative result from a diagnostic curettage is not 100% proof of the absence of carcinoma: for the uterus may be bicornuate.

(The chief practical lesson to be drawn from this case, as the author states, is that a serious error in diagnosis could occur if the existence of a bicornuate uterus is not recognized, and if the diagnostic curette happened to slip into the non-carcinomatous half of the uterus. This reminds me of one of the wild and woolly stories which the late Barton Cooke Hirst used to tell. On one occasion, in the days when small groups of medical students were permitted to make vaginal examinations during the progress of labor, Dr. Hirst asked one of the students, after his examination, to describe the condition of the cervix. The answer was that the canal was 2 fingers dilated. A student on the other side of the patient then made his examination, and reported that the canal was tightly closed. Several other examinations by students on alternate sides of the bed resulted in a tie vote on the two previous reports. Dr. Hirst's dénouement was, as may be surmised, that the patient had a double uterus and a double vagina, the fingers of one group of students slipping into one vaginal canal and those on the other side into the other.—Ed.)

SARCOMA OF THE UTERUS

F. H. MAGNEY

Duluth, Minnesota

Minnesota M., 32: 613, 1949

The author reviews 7 cases of sarcoma of the uterus occurring at St. Mary's Hospital from 1925 to 1947, and reports one additional case. A study of the records at this hospital shows that sarcoma of the uterus constitutes 0.54% of uterine malignancies. One of the patients survived over 12 years after operation, another over 4 years, a third over 2 years. The other 4 patients died within one year.

The case reported is that of a 48 year old woman, complaining of profuse

vaginal bleeding during menstrual periods. No bleeding occurred between periods. Pelvic examination revealed the body of the uterus to be the size of the head of a newborn. The uterus was freely movable and the cervix was normal. The clinical diagnosis was myoma of the uterus, with secondary anemia and tertiary syphilis. The bleeding was controlled by x-ray therapy over the pelvis. She was given antisyphilitic treatment, iron and thyroid. Two years later a subtotal hysterectomy was done. The tissues were vascular and friable. The histologic diagnosis was leiomyosarcoma of a grade II malignancy. Nine months after operation, there were symptoms of metastasis and the patient died eleven months postoperatively from generalized metastasis.

(Sarcoma of the uterus is only $\frac{1}{10}$ as common as carcinoma of the uterus, but it is as a rule more difficult of diagnosis than the latter. Biopsy of the cervix and thorough endometrial curettage will reveal carcinoma of either the cervix or the corpus in all but that group of doubtful early, often preinvasive stages which have excited so much discussion in recent years. With sarcoma, however, a preoperative diagnosis is uncommon except in the comparatively small group arising from the endometrium or endocervix, and therefore accessible to the curettage. For that matter, the diagnosis is in many cases unsuspected even at operation, especially in the considerable group in which the sarcoma originates in myoma. The surgeon who is familiar with gross pathology has a definite advantage in this respect, because sarcomatous changes can often, but certainly not always, be strongly suspected on cut section of myomas. Incidentally, it is well to cut into fibroids, and certainly those of soft feel, in the operating room, before the abdomen is closed. Most frequently fibroids of soft consistency are the seat of extensive hyaline and/or cystic degeneration, the surface having a homogeneous, rather gelatinous poorly trabeculated appearance, with often small or large cystic cavities. In the sarcomatous tumor the cut surface is likely to be pultaceous or of raw pork appearance, with sometimes ragged necrotic cavities. In any event, one can often be suspicious, and this suspicion will guide him in the extent of the operation.

One need not worry much about sarcoma if the cut surface of the tumors is hard, glistening and characteristically whorl-like and trabeculated. Failure to take such simple precautions explains at least some of the postoperative jolts which surgeons get when, several days after subtotal hysterectomy or myomectomy, the pathologist reports sarcoma. Whether to go back and complete the extirpation of the pelvic organs or to depend upon irradiation must be decided on such individual grounds as the histological type of the tumor, its location in relation to the line of uterine amputation etc. As a group the sarcomas arising in myomas offer a better prognosis than the diffuse intramural or endometrial varieties, but there are a good many exceptions.—Ed.)

CLINICAL REVIEW OF ENDOMETRIOSIS

W. B. WIENER

Jackson, Mississippi

Mississippi Doctor, 27: 26, 1949

Endometriosis is a disease of the childbearing age. In the last decade, there has been an increase in the incidence of endometriosis. Some claim that the increase

is due to the late age of marriage and the few subsequent pregnancies. The diagnosis of endometriosis will be made more often prior to surgery if one keeps in mind 3 points: (1) the cardinal symptom, dysmenorrhea; (2) the pathognomonic sign, the hard fixed nodule felt by recto-vaginal examination of the utero-sacral ligaments or peritoneum of the posterior vaginal vault; and (3) the special susceptibility of women sexually dormant.

It is sound surgical judgment to be radical in exploring all suspected cases. When the disease is found early, symptoms can be relieved and occasionally fertility restored by conservative surgery. To relieve symptoms where conservative methods are used, all lesions must be destroyed. The uterus should be suspended if not in normal position and the superior hypogastric nerve plexus should be removed. If this type of surgery can be done, 20 to 25% of the cases can be expected later to become pregnant. When pregnancy occurs after conservative surgery, the outlook for a normal prenatal course and delivery is as good as in any pregnancy.

(Of the 3 diagnostic points emphasized by the author, the second is much the most important. When a definite nodule or cluster of nodules is palpated in the uterosacral ligaments, there is little doubt that pelvic endometriosis exists. It is the presence of these nodules which often explains the dyspareunia of which many endometriosis patients complain, as well as the frequent reference of menstrual pain to the rectal, coccygeal or lower sacral regions. When operation is done for endometriosis, these utero-sacral implants may constitute a difficult problem. When small they can usually be completely destroyed with the cautery point or excised, but when they are large and associated with shortening and infiltration of the ligaments, it is sometimes impossible to feel sure that all endometrial tissue has been removed. This refers to the larger group of patients in whom conservative operation is indicated.

The problem is much simpler in those in which the extent of the disease, age of the patient, and the relative unimportance of conserving ovarian function justify radical operation. The complete removal of ovarian tissue brings about regression of the uterosacral involvement, usually making unnecessary any direct surgical attack upon the latter. All sorts of variations are encountered as regards the extent of the disease and the circumstances pertaining to the individual patient, and the judgment of the operator may be taxed in selecting the wisest procedure for the individual case. The late B. Z. Cashman urged supravaginal hysterectomy in the advanced cases in which it seemed impossible to remove all ovarian tissue and in which the age of the patient made subsequent irradiation impossible, and Counsellor in a recently published paper, expresses similar views (*Surg., Gynec. & Obst.* 89: 323, 1949). Certainly there is some sort of coordination between the endometrium and the ovaries, and it is possible that removal of the uterus may actually retard the growth of the ectopic endometrium, somewhat as the removal of the primary ovarian cancer is believed to retard the growth of peritoneal and other metastases. The evidence as regards the endometriosis cases is not yet conclusive, but it is a point to be borne in mind.

As for the diagnostic significance of dysmenorrhea, I believe this to be of relatively little importance unless combined with local palpatory findings. I have the impression that there are many who make the presumptive diagnosis of endometriosis in many cases of severe dysmenorrhea, apparently overlooking the very great frequency of primary dysmenorrhea. Some years ago, at a surgical meeting held in a university clinic in another city, the surgeon operated upon a woman who had severe dysmenorrhea and as I recall it, some dyspareunia. The surgeon said that although he could feel nothing definite in the pelvis, he felt sure that the patient had an endometriosis. Many of us in the audience were

not surprised that there was not the slightest trace of endometriosis, and the operator settled for what looked like an unnecessary suspension and appendectomy, not even including a presacral neurectomy, which would probably have been a far wiser compromise. The comments, which are not meant to be unkind or captious, serve to illustrate that dysmenorrhea is not likely to be due to endometriosis in the absence of some such pelvic finding as a tender and enlarged ovary which is adherent, usually very low in the pelvis, or nodules in the uterosacral region.

As a matter of fact, I have been impressed with the fact that not a few cases of unquestioned endometriosis, often of residual postoperative type, exhibit very little dysmenorrhea. It is to be remembered that pelvic endometriosis is in the majority of cases a relatively harmless disease, with almost no hazard of malignant change, and that many cases can be safely watched and kept quite comfortable by non-surgical means. In at least some of them pregnancy occurs. These remarks do not of course apply to more advanced cases where the pelvis is at times filled with the disease, with severe symptoms and such definite hazards as bowel obstruction.

Finally, the author's third diagnostic point, "the special susceptibility of women sexually dormant," is a very tenuous one, indicating his complete acceptance of the theory that celibacy and avoidance of pregnancy are of great etiologic importance. The chief basis for this, so far as I can see, appears to be the fact that the disease is more common in private than in ward patients. It is entirely possible that those who, like Meigs, have been urging the importance of this factor of sexual dormancy and making it the basis of an anti-birth control and anti-endometriosis campaign, are correct in their views, but it would seem to me that there are other variants than sex life which must be considered in the comparison between well-to-do private patients and the poorer ones of the ward type.—Ed.)

PRIMARY ENDOMETRIOSIS OF THE CERVIX UTERI

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Harper Hosp. Bull., 7: 195, 1949

Most endometriosis of the cervix is secondary to involvement of the recto-vaginal septum. Direct extension into the cervix from endometriosis of the uterine corpus has never been reported.

Only 6 cases of certain or probable primary endometriosis involving the cervix uteri have been reported. In contrast to this apparent rarity, the authors have encountered 4 instances in their personal practices within the past 9 years, and another one among the clinic patients at Harper Hospital.

Criteria favoring the diagnosis of primary endometriosis of the cervix, were as follows: (1) localization of the lesion on the anterior cervical lip or to one side of the external os; (2) an island of endometrial glands and stroma on the vaginal portion of the cervix, beneath the stratified, squamous epithelium, or exposed on the surface; (3) an endometrial island lying in the scar tissue; and, absolutely essential, (4) absence of any evidence of extension from endometriosis involving the uterus, recto-vaginal septum, or vaginal wall.

Pain is not a prominent feature in this disease; but abnormal bleeding is very frequent. If pregnancy co-exists, decidual change may occur.

The most likely origin of the lesion appears to be transplantation of endometrium to traumatized areas in the cervix. In the 11 reported cases, there was, without exception, a history of labor or operation as a cause of a traumatic site for implantation. In one case, the location of the lesions suggests implantation of endometrium in tenaculum punctures.

Endometriosis of the cervix superficially resembles carcinoma, and will frequently be associated with abnormal vaginal bleeding. Treatment is by eradication with the actual cautery or by excision. It is possible that endometriosis may bear some relation to adenocarcinoma of the cervix.

(As the authors state, primary endometriosis of the cervix is rare and we have encountered only a few instances in the material of our own laboratory. When we come to explaining the condition, we encounter the same still irreconcilable divergence of opinion which exists as regards the origin of the ordinary pelvic endometriosis. Whether implantation is the responsible factor, as the authors very plausibly maintain, or whether abnormal metaplastic changes in situ are concerned, cannot be definitely stated, and perhaps the mechanism is not always the same, as Sampson himself had come to believe in his latter years.

In this connection it is of interest that decidual transformation of the cervical stroma is not rare, and is certainly far more common than primary endometriosis. Nor is this cervical decidua merely a transformed endometriosis, as no endometrial glands are seen, only the stromal cells being involved. In this respect the cervical decidua is exactly like the islands of ectopic decidua so often seen on the back of the uterus, on the ovary, on the uterine ligaments and elsewhere in the pelvis, and also characterized by an absence of glands. These decidual changes are seen in the entire absence of genuine pelvic endometriosis, and certainly implantation plays no part in their origin. They can be explained only on the assumption that there are scattered areas in which the subperitoneal connective tissue cells retain a vestigial sensitivity to the progesterone which evokes the decidual transformation. A similar mechanism would seem to be the logical explanation of cervical decidua.

This could of course not be applied to the origin of ectopic cervical endometrium, but one can not forget that the distribution of ectopic decidua is practically identical with that of pelvic endometriosis, and that perhaps some local factor of persistent sensitivity is concerned in the etiology of both conditions, though no one knows what it is.—Ed.)

THE SURGICAL TREATMENT OF ENDOMETRIOSIS

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J. Oklahoma M. A., 42: 192, 1949

Endometriosis may be defined as the presence of endometrium in an abnormal location; it may be internal or external. Internal endometriosis refers to adenomyosis of the uterus, the presence of endometrial glands within the wall of the uterus. Cullen described 3 cases, and by serial sections, demonstrated that the endometrium invading the wall of the uterus was connected with the endometrium lining the cavity, thus of mullerian origin.

There are several theories of the origin of external endometriosis: retrograde

menstruation, fetal rests, metaplasia of epithelium in the pelvic peritoneum under the stimulus of inflammation, and lymphatic or blood metastasis. Retrograde menstruation explains the vast majority of cases, but not the occasional case of implants in the inguinal glands.

The findings most commonly associated with external endometriosis are: cervical stenosis, retroversion of the uterus in 50% of the cases, myomas of the uterus in 35 to 40% of the cases. The tubes are patent in the vast majority of cases and no salpingitis is present as a rule.

Palpation, culdoscopy and laparotomy are the methods by which endometriosis may be diagnosed; the history may be only suggestive. The earliest finding is thickening in the uterosacral ligaments; this thickening usually has a nodular character. The second early finding is the presence of b-b shot nodules in the cul-de-sac, palpable through the vagina or through the rectum. The ovary becomes densely adherent, but is of normal size. The differential diagnosis of the adherent ovarian cyst would be a tubo-ovarian inflammatory cyst, malignant cyst or endometrial cyst. The later form of the disease is the adenomyoma of the rectovaginal septum in which the b-b shot nodules become large, irregular masses filling the cul-de-sac.

Surgery is indicated for sterility, provided the endometriosis is definite and particularly if retroversion is present. Pain or bleeding is an indication for major surgery. Conservative surgery is indicated for all women under the age of 30 and all women under 35 strongly desirous of having children. The operation generally consists of dilatation of the cervix with curettage if there is menstrual abnormality. Attempt is made to excise all endometrial implants in the ovaries, uterosacral ligaments, cul-de-sacs, and sigmoid. Endometrial cysts in the ovaries are resected; myomas when present are excised. Suspension of the uterus is indicated in practically every case.

Radical surgery, removing both ovaries, tubes and uterus, is indicated in cases with extensive endometriosis. The ovaries are not routinely removed in patients over 35 years old.

The young woman with extensive endometriosis which cannot be excised, is treated with mild sedation and testosterone propionate. Certain cases with minimal residual endometriosis may be treated intermittently with estrogens and testosterone.

In 853 consecutive laparotomies, 250 cases of endometriosis occurred—an incidence of 29.3%. Radical surgery was performed in 37.2%, conservative operations with hysterectomy in 21.6%, and conservative surgery, maintaining the reproductive functions, in 41.2%. In the first group, 79.6% were over 35 years old; 51.6% had had one or more children. These patients complained of dysmenorrhea in 59.1% of the cases, and menometrorrhagia in 55.4%. Myomas of the uterus were found in 53.7% of the cases; retroversion occurred in 20.4%.

In the patients treated with conservative operations and hysterectomy, 70.4% were over 35. Fifty per cent of these patients had been delivered of children; 6 were unmarried which leaves a presumably sterile group of 38.8%.

Dysmenorrhea was the complaint of 66.6% of the patients; myomas were found in 61.1% and retroversion in 25.9%.

In the patients treated with strictly conservative operations, 77.6% were under 30 years of age. Previous pregnancy had occurred in 11.6%. Dysmenorrhea was complained of by 87.4%. Myomas of the uterus occurred in 16.4% and retroversion occurred in 59.2%. Subsequent pregnancy for the first time occurred in 33.8% of the married patients. The occurrence of pregnancy in one-third of the patients who had a conservative operation for endometriosis indicates the great value of such tedious dissecting operations.

In the conservative group of 103 cases, the electric loop was used to excise implants in 37. Suspension of the uterus is used in practically every case. Presacral sympathectomy was performed in 5.8%, giving fair results. Excision of implants with suspension as a rule, gives excellent improvement. It was felt that all of the endometriosis was excised in only 24.2% of the conservative group.

(This is an excellent appraisal of the subject by an experienced gynecologist, with statistical data on a large group of personal cases. His views are pretty much in accord with those now generally held, especially as to the wisdom of the conservative plan of treatment in the younger group of patients. Although his proportion of radical operations may seem a little high, 37.2 per cent, it is to be noted that 79.6 per cent of this group were over 35, and 51.6 per cent had had 1 or more children. In the conservatively treated cases, the removal of involved portions of the ovaries and the retention of uninvolved ovarian tissue is usually easy enough, but the troublesome part of such operations is the attempt to remove extra-ovarian endometriosis, especially in the uterosacral ligaments and rectal wall. It is not surprising that the author felt that all of the endometriosis was removed in only 24.2 per cent of the conservative group. The usual advisability of drawing the uterus away from the rectum by means of a suspension is stressed by Gray, but the proportion of these cases in which he does presacral neurectomy, 5.8 per cent, is much less than in my own practice. I believe this to be a valuable addition where dysmenorrhea has been an important symptom, as it so often is. See also comment on the two preceding abstracts.—Ed.)

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the female. On the other hand, if the Sertoli cells predominate, no endocrine effects will be observed in the female, but the male host will be feminized.

This explains why the most highly differentiated arrhenoblastomas of the ovary appear to exert no endocrine effect; the estrogen-producing Sertoli cells predominate.

(The author of this paper has made a number of valuable contributions to the comparative study of gonadal tumors of both the testis and the ovary, his chief thesis being the homology of certain groups in the two sexes. His previous studies on the 2 series of homologous tumors of the ovary and testis which he has postulated, the dysgerminoma and the androblastoma groups, have already been commented on in these pages. It is too soon to accept his conclusions in toto, especially as they are so largely based on morphological considerations, but it is becoming increasingly clear that one can scarcely acquire a broad biological concept of the dysontogenetic ovarian tumors without at least some knowledge of tumors in the corresponding embryological areas in the male.

In the present paper the author carries his concepts of homology still further, to the point of designating the ovarian *folliculome lipidique* as an androblastoma of tubular type. Granting that the sustentacular cells of Sertoli are probably the homologues of the ovarian granulosa cells, it still remains true that the latter are definitely and characteristically of feminine type, and that tumors composed of these cells exhibit characteristically feminizing effects. There would seem to be no more, and for that matter much less justification for including the tubular lipoidal varieties of granulosa cell tumor under the designation of androblastoma than to speak of the corresponding group of feminizing Sertoli cell tumors of the testis as a variety of granulosa cell tumor.

This is especially true when one considers that by far the largest number of cases of *folliculome lipidique* are not of tubular type. Similar lipoidal or luteinization changes are much more often seen in obvious granulosal tumors of more diffuse or cylindromatous patterns, so that it would be strange if such lipoidal transformations were not at times encountered in the far less frequent cases of tubular granulosa cell tumors.

The point I am trying to emphasize is that, with full appreciation of the probable homology of certain ovarian and certain testicular tumors, it would seem wiser for the present to retain the separate nomenclatures which have been built up for both, and that, until we know more than we now do, it would seem premature and a bit too revolutionary to try to blanket both groups in a single system of nomenclature. There are still too many mere hypotheses to justify this. For example, Teilum, in one of his previous papers, has urged that the lipoid cell tumors of the ovary which have been included under such designations as luteoma, adrenal cell tumors and masculinovoblastoma, are really to be looked upon as derived from the interstitial or Leydig cells of the testis. This may or may not be true, and, so far as I can see, the concept is based almost entirely on the undoubted morphologic resemblance of the constituent cells of many of these cells to Leydig cells. But this resemblance is no closer than it is to adrenal cells, and I personally believe that many, perhaps the majority, of tumors in this group are of adrenal character. Moreover, the embryologic rationale for such a view is sound, when one considers the embryologic contiguity of the adrenal cortex and the ovarian medulla.

The fundamental consideration on which Teilum's present paper is based, the homology of Sertoli cells and granulosal cells, has been given increasing support in recent years, and on this point there would be little basis for criticism. The homology is even more a functional than a morphologic one, since there now seems little doubt that it is these Sertoli cells of the testis which are responsible for the presence of estrogen in the urine of men. As far back as 1934 Zondek showed that the testis of the stallion is a rich source of estrogen (Nature, London 133: 209, 1934), and an increasing number of estrogen-producing testicular tumors is being reported, including a number observed in dogs. As these lines are written, a paper has just appeared reporting such a feminizing testicular tumor in a dog (Berthrong,

THE ADNEXA

ESTROGEN-PRODUCING SERTOLI CELL TUMORS (ANDROBLASTOMA TUBULARE LIPOIDES) OF THE HUMAN TESTIS AND OVARY. HOMOLOGOUS OVARIAN AND TESTICULAR TUMORS. III

GUNNAR TEILUM

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J. Clin. Endocrinol., 9: 301, 1949

In previous publications, the author has shown 2 series of homologous tumors of the testis and ovary: the dysgerminoma series, and the androblastoma series. In this study it will be shown that the feminizing tumors which have been designated as *folliculome lipidique* or granulosa cell tumor of tubular or adenomatous type are tubular androblastomas, despite their feminizing effects.

The author describes a case of feminizing androblastoma of the testis in a man aged 53 years. The tumor was intensely yellow macroscopically. Histologically, it showed all transitions from a diffuse blastema to well differentiated massive cords and tubules. If the trabeculae were cut parallel to their longitudinal axis, the tissue consisted of 2 rows of cylindrical cells with highly vacuolated cytoplasm. If the trabeculae were cut at right angles to their longitudinal axis, they showed a radial arrangement with transition to tubular cavities. The tumor was classified as an androblastoma tubulare (estrogen-producing Sertoli cell tumor).

The lipidic tubular portions of this tumor were found to be identical with the *folliculome lipidique* described by Varangot,¹ Traut, Henderson, Dougal and Greyle. Thus 8 cases of tubular, lipidic, macroscopically yellow, ovarian tumors have been collected from the literature. On the basis of morphological congruence with the feminizing androblastoma of the testis, these tumors may be histogenetically classified as androblastomas. This group does not belong to the granulosa cell tumors; rather, it arises from male-directed cellular material in which a differentiation tending in the direction of Sertoli and/or Leydig cells may take place, the hormonal effect of the tumor depending upon which type predominates.

Testis tumors with estrogen effects have been described in dogs; the estrogen appears to be derived from the Sertoli cells. The tumors of feminized dogs contained large amounts of lipoid. By definition, the cells of the testicular tubules with high lipid content are Sertoli cells. Various other authors have postulated that the testis, by means of the Sertoli cells, produces a hormone similar to estrin. The Sertoli cell tumors in dogs are morphologically identical with the androblastoma testis previously described. A gonadal tumor with complete dominance of Leydig cells will give no symptoms in the male, but will virilize

type. My own impression is that the figure is closer to 25 per cent than 12.7 per cent. We are hoping that the study of the rapidly accumulating material of the Ovarian Tumor Registry, already containing a considerable group of arrhenoblastomas, will permit of more accurate appraisal of the degree of malignancy of this type of neoplasm. The authors of the above paper are herewith invited to send representative slides and clinical data of their case for inclusion in the Registry.—Ed.)

OVARIAN TUMORS IN INFANCY AND CHILDHOOD

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J. Lancet, 69: 160, 1949

Over 200 ovarian neoplasms have been reported in the pediatric literature. Approximately 60% of these have been of the solid malignant variety; about 20% are dermoids; and about 20% are simple cysts. Over a 3 year period, the authors have treated six cases of ovarian tumors in children ranging from 4 months to 16 years of age.

Cystic tumors of the ovary may be detected as discrete abdominal masses on routine examination. These tumors attract attention by intermittent lower abdominal discomfort, by progressive enlargement of the abdomen and by acute abdominal pain resulting from torsion of the pedicle. Simple cysts contain a clear amber fluid and dermoids contain hair, sebaceous material, teeth and other ectodermal elements.

The authors report 3 cases of cystic tumors of the ovary: a paraovarian cyst, an ovarian cyst, and a dermoid cyst. Excision of cyst, salpingo-oophorectomy, and oophorectomy were performed with uneventful convalescence in each case.

Benign solid tumors of the ovary are rare in childhood. Of the malignant solid tumors, the teratomas are the most common. Of the functioning tumors, the feminizing granulosa cell type is the most common. The clinical features of the solid tumors are an enlarged abdominal or pelvic mass and endocrine dysfunctions consistent with the ovarian tumor types. Pain is rare unless torsion has occurred.

The authors report 3 cases of solid ovarian tumors: ovarian teratoma, ovarian sarcoma, and arrhenoblastoma. The patient with ovarian teratoma was a 9 year old female admitted for lower abdominal pain of 3 days' duration. At operation a solid left ovarian tumor was removed. The follow-up has been satisfactory for 2½ years.

A 5 year old female was admitted with pelvic pain of 3 weeks duration. There was a non-painful swelling behind her left ear. Pelvic examination revealed a freely movable right adnexal mass. At operation, bilateral oophorectomy was performed. Sections showed that both ovarian masses and the cervical nodes were involved with rapidly growing sarcoma. The patient died a few months after operation.

Goodwin and Scott, *J. Clin. Endocrin.* 9: 579 (July) 1949), and collecting from the literature a number of previous cases of this sort, in both dogs and humans. To those interested in the general subject, a reading of this paper should be interesting and profitable.—Ed.)

ARRHENOBLASTOMA

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West. J. Surg., 57: 235, 1949

The patient was a 20 year old woman admitted June 13, 1945 with complaints of amenorrhea, change in voice and growth of a beard. Menses had been painless and profuse. The last menstrual period was January 14, 1944. On examination, the uterus was small, the left ovary was solid, freely movable and about 5 cm. in diameter. The right adnexa felt normal. The clitoris was moderately enlarged. No abdominal masses were felt. On June 19, 1945, the left ovary, the left tube and the appendix were removed. There were no other gross abnormalities. The ovary was replaced by a smooth, semisolid tumor and was covered with a gray capsule. On bisection, 3 nodules, surrounded by many hemorrhagic, cystic areas were found. The adjacent fallopian tube appeared normal. Microscopic examination of the tumor revealed fibrillar stroma containing islands of interstitial cells in some places. Elsewhere, there were tubular structures surrounded by spindle cells, some of which were arranged in whorls and columns. The tumor was regarded as an arrhenoblastoma of the intermediate type.

The postoperative course was satisfactory. One month postoperatively a normal menstrual period began. Two years later the patient became pregnant and delivered a normal child. Forty-two months postoperatively there was no evidence of recurrence of the tumor.

Conservative treatment appears desirable among women of reproductive age. With the known rate of recurrence (12.7%), it is apparent that conservative treatment is advisable only if the affected ovary is free and by histologic study the tumor is encapsulated with no clinical evidence of metastases. Removal of both adnexa and the uterus is the procedure of choice during the menopausal and postmenopausal age.

(The description of the microscopic picture and the clinical course would seem to leave no doubt as to the correctness of the diagnosis. I get the impression from the gross description that the tumor was multiple, since "3 nodules" are described. This would be unusual but not unique. For example, an interesting example of multiple arrhenoblastoma was reported by Gnassi in 1936 (*Am. J. Obst. & Gynec.*, 31: 135, 1936).

The authors speak of the "known rate of recurrence (12.7 per cent)" but I do not believe that the recurrence rate is as yet known with any degree of accuracy, simply because not enough reliable follow-up studies are as yet available concerning this relatively rare tumor

PERITONEAL BODIES AND CYSTS OF THE BROAD LIGAMENT

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Am. J. Obst. and Gynec., 57: 890, 1949

In 1903, Walthard published a paper concerned with epithelial inclusions in the ovary. He described 2 ovaries which contained small solid epithelial bodies, noted that similar structures were found in and under the serosa of the tube, and stated that they may undergo cystic changes in this location.

Routine slides of one or both salpingo-oophorectomy specimens from 150 patients were examined. The lateral half of the tube, broad ligament and ovary from 16 patients were serially sectioned and studied. These solid or cystic structures were noted in specimens from 78 patients.

The solid bodies are composed of a mass of epithelial cells with distinct cell membranes, faintly staining cytoplasm, and vesicular nuclei with little or no chromatin. There are no intercellular bridges, no basement membrane and no true capsule. Cavity formation and cystic dilatation can be observed in various specimens. In the larger cysts, the epithelium consists of two layers of flattened cells.

The impression is current that these structures are found only on or just beneath the serosa of the tube. Of 67 solid or cystic bodies whose position could be accurately determined, 33 were on the tube and 34 on other areas of the broad ligament. In this latter location, 9 were on the mesovarium and 25 on the mesosalpinx. A few of the solid bodies showed direct continuity with the mesothelium, a few were just subserosal, still others were noted to be separated from the serosal surface by a definite layer of connective tissue. This was also true of bodies that showed cystic dilatation. Thirty-five patients were studied for evidence of inflammatory reactions; it was found in 32 specimens.

Peritoneal bodies and peritoneal cysts may be differentiated from cysts of mesonephric or paramesonephric origin by the absence of a true capsule. The epithelium of peritoneal cysts is composed of flattened cells, usually two layers in thickness.

Four main theories have been proposed to explain the histogenesis of peritoneal bodies. Rossa (1898) thought that they arise from accessory adrenal tissue. Schickele (1902) believed that they develop *in-situ* from surface epithelium. This surface epithelium, however, was not peritoneal mesothelium, but ovarian germinal epithelium which had migrated to an aberrant location in an unknown manner due to an unknown stimulus. Reis suggested that they develop from misplaced entodermal cells of cloacal origin. Werth (1887) showed that these bodies develop as proliferations of the peritoneal epithelium. Meyer (1903) showed the early stages of proliferation of the peritoneal epithelium. He concluded that these bodies occur as a response by the peritoneum to inflammatory processes.

A 16 year old female was admitted with history of amenorrhea of 2 years duration, hirsutism, and an enlarging abdominal mass. At surgery, a well-encapsulated left tubo-ovarian tumor was removed which weighed 8.2 pounds. Sections showed male testicular architecture consistent with arrhenoblastoma. One year later, the patient had recurrence of symptoms. At operation, tumor implants were removed from the omentum, visceral and parietal peritoneum and the left broad ligament. Sections showed mostly striated skeletal muscle fibers. X-ray therapy was carried out; the patient is still alive but the prognosis is poor.

(The comparatively recent recognition of the dysontogenetic group of ovarian tumors has made it necessary to reappraise the neoplasms previously reported in infancy and childhood. Many of the tumors formerly looked upon as sarcomas we would now diagnose as granulosa cell tumors or dysgerminomas. It is of interest that a number of cases in the older literature were reported as sarcomas in association with precocious puberty. I had occasion many years ago to review some of these publications and often it was quite certain from the photomicrographic illustrations that the tumors were granulosal and not sarcomatous. In other cases reported as sarcoma and not associated with precocious puberty, the tumors were obviously dysgerminomas. This does not mean that sarcomas also may not occur in very early life, because of course they can, though not so frequently as was once believed.

When a solid tumor of the ovary is found in an infant or child, therefore, it is reasonably sure to be a granulosa cell tumor, dysgerminoma, sarcoma or teratoma. The first of these may be assumed if the precocious puberty syndrome is present. On the other hand, one is not justified in assuming the presence of a granulosa cell tumor with an existing precocious puberty syndrome unless such a tumor can be palpated. Far more frequently the precocious symptoms are of so-called constitutional type, with no tumor present either in the ovaries or in any other endocrine gland (Novak, *The constitutional type of female precocious puberty*. Am. J. Obst. & Gynec. 47: 20, 1944).

The finding of a solid ovarian tumor in a child, therefore, is always a matter of concern, since all the types above enumerated are potentially or very actively malignant, the latter applying especially to the sarcomas and teratomas. In the teratoma reported by the authors the patient was well 2½ years after operation, but with most such tumors recurrent metastasis and death have occurred, sometimes with amazing rapidity. Incidentally, I note that the metastases in the case of arrhenoblastoma reported by the authors showed "mostly striated skeletal muscle fibers." This would make one suspect that the arrhenoblastoma was associated with teratoma, such a combination having been noted in quite a number of cases. The first case of arrhenoblastoma reported in this country, that of Taylor, Wolfermann and Krock (*Surg., Gynec. & Obst.* 56: 1040, 1933), was of this type and the metastases which occurred in this case likewise showed teratomatous elements.—Ed.)

The main symptom of pelvic inflammatory disease is pain in the lower abdomen. The signs of the condition are temperature elevation, rigidity, tenderness, and muscle spasm; and pain and tenderness of the internal genitalia upon examination.

The causes of this condition may be divided into 2 groups: those of bacterial origin, and those caused by physical forces. The former are the gonorrheal, the septic, and the tuberculous. The mycoses are also recognized causes; there are undoubtedly others which have been unrecognized. The physical changes in the pelvic viscera which may cause pelvic inflammation are almost unlimited; some of them are twisted tumors, degenerating myomas, and ruptured ectopic pregnancies.

Pelvic inflammatory disease of infectious origin is distributed either by surface extension or interstitial extension. The former type originates from an endocervicitis, a urethritis, or a Bartholinitis. It is usually transmitted to the upper genital tract by some physical force. The organisms extend along the mucosal surfaces of the various pelvic structures. There is lower abdominal pain, muscle rigidity, a high temperature and leucocytosis. The clinical reaction lasts about 72 hours and in many instances spontaneous and almost complete resolution occurs. These attacks tend to recur because of a latent lower genital infection. With each reinfection, some change occurs in the pelvic structure; eventually pelvic abscesses, adhesive changes, and pyosalpinges develop. These reactions have commonly been attributed to the gonococcus. The latter, however, has not always been the cause. Pelvic inflammation by interstitial extension is most frequently associated with the streptococcus and staphylococcus. The organism is inoculated into a break in the surface of the genital tract and may therefore follow any trauma, such as curettage, cauterization, or spontaneous interruption of pregnancy. Septic infections are most frequently puerperal. They progress by way of the lymphatic and cellular tissue of the pelvis. They are frequently self-limited; occasionally an abscess may develop. In a few instances, generalized peritonitis or septicemia may develop.

Tuberculous pelvic inflammation is truly chronic. It probably develops from a focus of tuberculosis elsewhere. It may be either a surface or an interstitial process.

Pelvic inflammation due to physical causes is often confused clinically with that of bacterial origin. The author cites 2 cases to illustrate this point. In the first case, the patient, a Negro, was thought to have chronic pelvic inflammatory disease. Actually, she was bleeding from a granulosal cell tumor, and the inflammation was due to free blood in the belly. The second patient had a cystadenoma of the ovary, which had ruptured, producing acute symptoms.

Pelvic inflammatory disease is an entity because of the anatomic and physiologic characteristics of the female. The inherent reaction of the individual to the process is not much different in the female pelvis than in other regions.

(The views expressed in this paper are in accord with those generally held concerning pelvic inflammatory disease except on the point of the author's division into 2 groups. The usual connotation of the term "pelvic inflammatory disease" is an inflammatory process involving primarily the genital tract and including some degree of tubal involvement. For

The authors' findings were similar to those described by Werth and Meyer. In 3 of the specimens, there was no evidence of inflammation. It is conceivable that the bodies may arise as the result of chemical irritation.

Solid epithelial bodies in the ovary similar to those found under the serosa of the tube and broad ligament are very rare. The authors found no solid bodies and no cystic derivatives in the ovaries of the routine sections. In serial sections, 2 solid epithelial bodies were found.

(The authors of this paper have apparently gone all out for reform in nomenclature. Without meaning to discourage them, and without meaning to be cynical, I am afraid that their little crusade will be somewhat like Don Quixote's campaign against the windmills. As I have previously remarked in these pages, the way of the reformer in the field of medical nomenclature, as in most others, is a hard and discouraging one. In a recent paper the same group urged that the Muellerian ducts be henceforth spoken of as parmesonephric, to distinguish them from the mesonephric or wolffian ducts, but I predict that the eponymic designations will not be abandoned in the foreseeable future, just as we shall continue to speak of McBurney's point, Wharton's jelly, Langhans' cells, etc. This rather pessimistic statement is made with full appreciation of the general undesirability of the eponymic plan, and of the fact that the man whose name is thus perpetuated is not always the one who deserves this sort of scientific memorial.

As regards the cell islets and the "peritoneal cysts" described in the present paper, somewhat the same comment can be made. Even though the cell nests were originally described by Werth, and possibly by some one else even before Werth, the designation of Walthard islets has become so entrenched in the literature that I doubt that it will be dislodged. As a matter of fact, sporadic efforts at thus reforming the nomenclature are apt to cause such confusion that it may be questioned whether it is not better to bear the ills we have than fly to others we know not of.

As the authors state, the Walthard islands (just to be stubborn) are much more frequently seen in the tubes than on or just beneath the ovarian surface, but I would not think, from my own experience, that the ovarian situs is nearly as rare as the authors find it. They mention the various theories as to their origin, but none can be established beyond doubt. I do not believe that inflammation is nearly as important as the authors do. Again, I do not feel sure that all of the peritoneal cysts which they describe are to be linked up with Walthard nests. Simple inflammatory peritoneal cysts are not rare, and the lining peritoneum not infrequently shows metaplastic changes, with sometimes stratification, which may wrongly be interpreted as a cystically degenerated Walthard island.—Ed.)

A STUDY AND CLASSIFICATION OF PELVIC INFLAMMATORY DISEASE

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Am. J. Obst. and Gynec., 57: 1077, 1949

Pelvic inflammation involves the uterus, adnexa, parametria, pelvic peritoneum, and sometimes the rectum, sigmoid, and cecum. During the procreative period, the female genital tract is patulous and there is a normal communication between the external environment and the peritoneal cavity.

FEMALE UROLOGY

URINARY TRACT CHANGES IN CERVICAL CARCINOMA

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Surg., Gynec. and Obst., 87: 705, 1948

A high incidence of urinary tract disease associated with cervical carcinoma has been noted. Thirty-seven patients with cervical cancer were studied to determine the status of the urinary tract before and after radiation therapy. The ages of the patients ranged from 25 to 75 years; the average age of the group was 50 years. In 29% of the patients, the carcinoma was confined to the portio of the cervix; in 24% there was spread of the disease process to the vaginal vaults; the remaining 47% showed parametrial involvement.

All cervical cancer patients at the University of Maryland Hospital are studied by biopsy and examination under anesthesia. The tumor is graded microscopically, by the method of Ewing, and clinically, by the method of Schmitz. Most patients receive 3,000 mg. hours of radium as an initial dose. The same dose is repeated 3 weeks later. Heavy filters at the extremities of the radium tubes and meticulous vaginal packing are utilized to protect the bladder, ureters, and rectum as much as possible. Three weeks following conclusion of radium therapy a cycle of deep x-ray therapy totalling 6,000 to 8,000 r is given and repeated 12 weeks later.

Prior to therapy, all patients had a complete urological study, using water cystoscopy and retrograde pyelography. The transverse diameter of the ureter was measured at the level of the ischial spines, the lower junction of the ilium and sacrum, and at the level of the transverse process of the 3rd and 4th lumbar vertebrae. The contour of the kidney pelvis was also noted. One year following the completion of all therapy, the same urological study was repeated.

Prior to therapy, 27% of the patients showed some degree of urinary tract dilatation. The urinary tract dilatation was much commoner and more extensive among patients with advanced carcinoma and parametrial spread. At the end of radiation therapy, 38% of the patients showed some degree of hydronephrosis or hydroureter; 79% of those having dilatation following therapy also had extension of the malignancy. No patient with a carcinoma of grade I developed urinary tract dilatation between examinations. Moreover, no patient with a grade II carcinoma developed dilatation. Patients with grade III carcinoma were the only ones to develop urinary tract dilatation during the interval between examinations. All patients who showed an increase in the hydronephrosis and hydroureter, showed a definite spread of the disease in spite of therapy, and subsequently died of the malignancy.

example, I do not believe that most of us would speak of a trichomonas vaginitis or a simple urethritis or a chronic cervicitis as pelvic inflammatory disease, though these lesions of localized genital tract segments are definitely inflammatory. The common "p.i.d." of hospital histories refers to a more extensive and diffuse process involving the tubes and usually pelvic peritoneum. The term is a rather loose one, which appears to have become popular, more or less as a matter of convenience, and although I do not recall ever having seen a definition of any sharpness or precision, I do believe that both acute and chronic "p.i.d." have in most clinics come to be applied to the rather diffuse and intrapelvic inflammations, and that these terms do not in the minds of most of us apply to localized inflammation of the lower genital region, though the latter is not infrequently a part of the more general pelvic inflammatory process. These remarks are not a criticism of the author's paper, because whatever one may believe to constitute the acute or chronic pelvic inflammatory disease syndrome, a description of the involvement must include description of the involvement of different segments of the canal. The accepted cause is bacterial, and the author's subdivision into the gonorrheal, septic and tuberculous groups is the one generally accepted.

As to his second group, those caused by physical forces, there will be more question. Any pelvic inflammation produced by such adventitious factors as twisted tumors, degenerating myomas and ruptured ectopic pregnancies, if of only circulatory or chemically irritative nature, is apt to be so slight that we would not wish to include it in the concept of pelvic inflammatory disease. When inflammation is more outspoken, with perhaps sup-puration, bacteria are always involved, and the case belongs to the generally accepted bacterial group. In short, the only point I raise, and it is one of purely individual viewpoint, is as to the wisdom or necessity of including the author's second group in our concept of pelvic inflammatory disease.—Ed.)

The authors report the 11th case of solitary pelvic kidney associated with absence of the vagina. The patient was a 34 year old woman, admitted because of intermittent nonradiating abdominal pain. The pain was accentuated at monthly intervals and during coitus. She complained of urinary incontinence following coitus and slight stress incontinence. She had been married for 7 years but had never menstruated nor been pregnant. At physical examination, the kidneys were not palpable in the flanks. There was some tenderness in the suprapubic area. On pelvic examination, she was found to have complete absence of a true vaginal orifice and introitus. Between the labia majora there was a blind pouch covered by rugous epithelium which extended posteriorly into the urorectal septum. No cervix or uterus was palpable. Entering the superior surface of the pouch was a finger-sized opening, thought to be the urethral orifice. The inner surface of a musculo-membranous structure could be palpated and this was interpreted as bladder. Excretory urograms revealed a well-functioning solitary ectopic kidney located well within the pelvis. An artificial vagina was created by the Frank non-operative method. A depth of $3\frac{1}{2}$ inches was attained with which the patient is able to have satisfactory painless coitus. After this procedure, the patient no longer had stress incontinence and catheterized urine specimens were normal.

(Although the authors were able to collect only 11 cases, including their own, of solitary pelvic kidney in association with absence of the vagina and uterus, it must be remembered that other and less serious types of urinary tract anomaly are much more frequently combined with congenital anomalies of the reproductive apparatus. Such abnormalities as horse-shoe or double kidney, and partially or completely double ureter and kidney pelvis are not infrequently found in such cases. It is easy to see that a solitary pelvic kidney might confuse the diagnostic picture. Not only might the kidney be mistaken for a uterus, as the authors state, but if it is enlarged by hydronephrosis which not infrequently develops in ectopic kidneys, there would be a pretty close palpatory simulation of an adnexal mass. The rather crucial value of pyelographic studies in such cases is evident, and, for that matter they should be a routine part of the examination of patients with congenital anomalies of the reproductive apparatus.—Ed.)

THE SURGICAL ANATOMY OF CYSTOCELE AND URETHROCELE WITH SPECIAL REFERENCE TO THE PUBOCERVICAL FASCIA

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Surg., Gynec. Obst., 87: 725, 1949

The pubocervical fascia is described as an anatomic entity by many gynecologists. It is believed that a congenital defect in, or obstetric injury to this fascia is the basic cause of cystocele and urethrocele.

Everett (*Am. J. Obst.*, 28: 1, 1934) has maintained that in time, half the patients treated by irradiation for cervical cancer, will develop some degree of ureteral stricture. In order to eliminate radiation effect, the ureter must receive maximal protection as it courses near the cervix. Upward traction on the uterus during a hysterectomy increases the distance between the cervix and ureters, minimizing the danger of injury to the latter. In radiation therapy, maximum accurate vaginal packing achieves the same result. By vaginal packing, the authors were able to increase the distance between the cervix and the most vulnerable portion of the ureter by as much as 8.5 cm.

The authors have estimated the maximal dosage of radiation to various portions of the pelvic ureter. At no point in its course through the average pelvis was the ureter exposed to more than 34-45 mg. hours of exposure. In dogs it has been shown that doses of less than 50 mg. hours of radiation to the ureters produce very little stenosis.

The authors conclude that radiation therapy will not cause ureteral stricture if the dosage is not excessive and the source of the ray is displaced from the ureter by maximal vaginal packing.

(It is a well-known fact that urinary tract dilatation and obstruction are frequently found in patients following radiological treatment of cervical cancer, but there is often difficulty in deciding whether such changes are the result of the therapy or the result of the infiltrating progress of the disease, especially since the latter factor in itself has long been known to produce ureteral blockage and ultimately uremia in perhaps the largest proportion of cases progressing to a fatal termination.

The especial virtue of the paper abstracted above is that it is based on pyelographic studies made both before and after the institution of radiotherapy. Radiologists will no doubt find consolation in the conclusions of the authors that at least a considerable proportion of ureteral obstructive lesions reported after radiotherapy are really not due to the latter, but they should still heed the admonitions of the authors as to the importance of getting the ureters out of the danger zone of radiotherapy, just as the surgeon must constantly be on his guard against injuring these structures in his operative attacks on cervical cancer.—Ed.)

SOLITARY PELVIC KIDNEY WITH VAGINAL APLASIA: REPORT OF A CASE

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J. Urol., 61: 862, 1949

Only 10 cases of solitary pelvic kidney associated with absence of the vagina have been reported. A total of 42 cases of solitary pelvic kidney have been reported. A complete urological study is important in any case of vaginal aplasia. In the absence of vagina and uterus, a pelvic kidney can easily be mistaken for the uterus.

OPERATIVE GYNECOLOGY

THE SURGICAL PROBLEM OF RECURRENT AND UNCONTROLLED CANCER OF THE FEMALE GENITALIA AFTER PREVIOUS IRRADIATION AND CONSERVATIVE SURGERY

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Cincinnati J. Med., 30: 243, 1949

At the Memorial Hospital, a surgical program to attempt a salvage of patients with cancer of the cervix, persistent or recurrent, after failure of irradiation therapy, has been initiated. The patients may be classified into 4 groups: (1) patients with cervical carcinoma limited to the cervix and immediately adjacent areas, (2) patients with recurrent carcinoma that has involved the bladder, (3) those with cervical carcinoma involving the pelvic colon, and (4) patients with cervical carcinoma involving both the rectum and bladder.

Radical panhysterectomy with pelvic lymph node dissection was performed on 27 patients in group 1; there was no surgical mortality. Fourteen patients were living and well without evidence of recurrence 3 months to over one year after operation.

Total cystectomy, hysterectomy and vaginectomy was performed on 21 patients in group 2; surgical mortality was 6. Six patients were living and well without evidence of recurrence up to 13 months after operation.

A radical one-stage procedure was performed for excision of all pelvic viscera on the patients in group 4. An end colostomy with implantation of the ureters into the upper sigmoid above the colostomy was performed. Forty-eight patients were subjected to this procedure. There were 12 surgical deaths; 14 patients were living and well without evidence of metastases, and 4 patients were living and well for one year or more.

(The recent swing-back to radical surgery in Stage 1 and some Stage 2 cases of cervical cancer has been fully justified in the minds of many by the remarkable lowering in primary mortality as a result of such modern surgical resources as transfusion, antibiotics and sulfa therapy. Aside from this there would seem to be no reason to expect any very noteworthy improvement in salvage rates over those obtained by comparable operations in the hands of expert surgeons in preradiation days. It should not be many years before such arm-chair philosophizing can be checked in the light of the reports which will begin to come in from those who have embarked on the surgical plan for the early group of cases.

This comparatively conservative surgical plan, however, is quite different from the very radical surgical plan now advocated by Brunswick and the Memorial Hospital group. In this respect Brunswick has out-Heroded the Herods of both the present and the past. I have not the slightest doubt that up until a couple of years ago the idea of radical operation in a far advanced presumably hopeless case of cervical cancer would have been thrust aside

The anterior vaginal wall is fused intimately with the posterior urethral wall. At a higher level, a line of natural cleavage exists between the muscular coat of the vagina and that of the bladder. Similar relations exist posteriorly with the anus and rectum. Laterally, the vagina is attached to the endopelvic fascia.

The bladder is fixed interiorly by its true ligaments. The latter are derived from the pelvic fascia; there are 2 lateral and 2 anterior. The urethra is attached laterally to the endopelvic fascia. Superiorly, it blends with the musculature of the bladder wall; inferiorly, it is attached to the urogenital trigone. Anteriorly, the urethral wall is attached to the connective tissue in the floor of the space of Retzius.

Histologic investigation of the vaginal wall shows that it consists of a mucous, muscular, and fibrous coat. The bladder wall has 4 coats: the mucous, the sub-mucous, the muscular, and the fibrous. The urethral wall consists of mucous membrane supplemented by an outer muscular tunic. No histologist has ever described a layer of fascia in the walls of the vagina, urinary bladder, or urethra.

There is no fascia between the wall of the urethra and the wall of the vagina; the only fascia between the bladder and the vagina is a single loose areolar layer.

If cystocele or urethrocele exists, the vaginal wall is hypertrophied in all its layers, this hypertrophy being proportional to the degree of the cystocele. The term "pubovesicocervical fascia" has been incorrectly applied to the hypertrophied muscular coat of the vaginal wall in cystocele. This muscular wall histologically is not a fascia in any sense of the term.

The author concludes that there is no pubocervical fascia in the human pelvis. A new concept of the etiology of cystocele and urethrocele must accordingly be developed.

(An excellent anatomical study with conclusions as to the muscular rather than fibrous structure of the so-called pubocervical fascia similar to those reached by a number of other investigators during the past few years. However, the fact that this firm and dense layer is not fibrous, as formerly believed, does not lessen the value of its utilization in plastic operations for the correction of cystocele.—Ed.)

than from within the peritoneum. This is especially true in the obese patient. The mortality has been 4%. There have been 2 deaths from pulmonary embolus. The sole consideration in the selection of cases for this operation revolves about the evaluation of the chance of total cure within 3 or more months after completion of a full course of radiation therapy. This estimate is based upon clinical appraisal, vaginal smear, and biopsy. This estimate is sometimes wrong; in 14% of the cases, the disease recurred locally following gland dissection. An overall finding of 28% of positive nodes following complete radiation has been observed by the authors. The authors do not attempt to draw any conclusion. They feel that the series is too small and too recent to justify extended observations.

(The description of this 2 stage operation would seem to justify the hope of the authors that it may offer definite advantage over the plan of radical abdominal hysterectomy plus abdominal gland dissection. The peritoneal plan of gland removal suggested by Nathanson is much like that employed in the Basset operation for carcinoma of the vulva, and would seem to offer a better approach than the abdominal one. The authors warn against drawing any premature conclusions as to the results of the operation devised, just as they have been cautious in drawing too early conclusions from the radical abdominal operation which they have practised in a large group of cases. It should not be many years before some sort of idea can be gained as to the comparability of 5 year cure rates in the surgically treated cases with those treated by irradiation alone.—Ed.)

EXCISION OF THE ROUND LIGAMENTS IN CORPOREAL AND OVARIAN CARCINOMA

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J. Obst. and Gynaec. Brit. Emp., 56: 226, 1949

A lymphatic communication between the body of the uterus and the glands of the groin along the course of the round ligaments has long been recognized. It would seem a sensible precaution to remove both round ligaments and the surrounding cellular tissue as far as the internal ring in every radical operation for uterine or ovarian cancer. Such a step presents no technical difficulties, adds nothing to the severity of the operation, and might lessen the risk of recurrences.

The author presents 2 cases of corporeal cancers and one case of papillary adenocarcinoma of the ovary. The 2 cases of corporeal cancers were early growths, confined to the body of the uterus, treated by total hysterectomy with removal of both appendages and wide excision of the broad ligaments. After one and 3 years respectively, the patients were found to have secondary growths invading the rectus muscles and the aponeurosis of the oblique muscles. The patient with primary papillary adenocarcinoma of the ovary was treated by total hysterectomy with wide excision of both appendages. One year later the patient returned

as unjustifiable and perhaps almost criminal by virtually all gynecologists. And now Brunswick has brought this plan into the realm of serious thought and discussion. Here again the arm-chair philosopher will have to restrain his irritation and impatience and wait to see whether the end justifies the heroic means; whether, in other words, the amelioration of the advanced cancer patient's lot is sufficient to justify such radical procedures as total removal of the genital organs, bladder and rectum, especially when a high primary mortality is inevitable even in the hands of the most expert surgeon with the most complete surgical equipment and resources at his command. Here again we shall just have to wait and see.—Ed.)

RETROPERITONEAL LYMPH NODE DISSECTION IN CANCER OF THE CERVIX

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Am. J. Obst. and Gynec., 57: 1087, 1949

Approximately 60% of all patients with cancer of the cervix die. The majority die with the disease still confined to the pelvis. Eighty per cent of the cases of cancer of the cervix have extended beyond the cervix proper when they are seen.

Radiation therapy is reasonably effective in so far as the original lesion goes. However, there is serious doubt as to the efficacy of x-ray therapy in dealing with extension of the disease, obturator, hypogastric, and iliac nodes. The extent of regional node involvement in cervical cancer is unknown. In a group of Stage I cases operated upon by Meigs, 17% were found to have involvement of the regional nodes.

The authors are now making a surgical attack upon the regional nodes after there is a reasonable assurance that the local disease has been cured. No attempt has been made to alter the established plan of radiation therapy. The portals of entry include the nodal areas despite the fact that these regions will later be exposed to surgery.

The operation is performed in 2 stages at weekly intervals. An incision is made as for a herniorrhaphy and carried down to the peritoneum. The latter is stripped upward and medially. Beginning at the inguinal ligament, the nodes along the common iliac artery to the bifurcation of the aorta are stripped clean. The dissection is then carried down the hypogastric artery, cleaning out the space between the junction of the 2 vessels. The obturator area is reached by identifying the obturator nerve as the external iliac vein is retracted laterally. The depth of the dissection is marked by the anatomical position of the nerve. The fatty tissue is removed until the bare bone of the bony pelvis is seen. The wound is then reconstructed as in the herniorrhaphy.

The authors find that it is easier to attack these nodes extraperitoneally

vessels being pretty husky, so that I personally prefer to tie these larger spurters, instead of depending on a puckering suture as does the author. Some of these cysts are the result of blockage and distension of the main duct, others arise from similar obstruction of one of the subdivisions of the duct, so that they involve only one lobule of the gland. The practical point is that the whole gland and not just the cyst should be removed, since residual gland tissue is quite surely infected and may give rise to later recurrence of cyst or abscess. One usually tries to remove the gland without rupturing the cyst, but this is not always possible, as the thin wall of the latter may be practically incorporated with the skin. Often enough the cyst is neatly dissected out without rupture until almost complete removal and then the thin wall squashes. The removal of a large cystic gland leaves a rather large hole which oozes freely even after ligation of the bigger vessels. The cavity is best closed by a number of puckering stitches, but no matter how careful one is about hemostasis and skin suture, the wound is likely to heal by granulation rather than by first intention.—Ed.)

RADIUM THERAPY FOR CARCINOMA OF BARTHOLIN'S GLANDS

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Am. J. Roentgenol., 61: 517, 1949

Between January 1910 and December 31, 1947, 700 benign lesions of Bartholin's glands were treated at the Mayo Clinic. During the same period, 7 primary malignant growths of the gland were found, an incidence of 1%. Between 50 and 90 cases of carcinoma of Bartholin's glands have been reported in the literature. Carcinoma of the gland invades deeply, involving fat, muscle, and the pubic bones; the tumor metastasizes to the inguinal nodes in at least 50% of the cases. Both adenocarcinoma and squamous carcinoma occur; the former predominates by about 2.5 to 1.

The authors report 7 cases treated between 1924 and 1940. Five lesions were squamous cell epitheliomas and 2 adenocarcinomas. Most of the lesions were of a low grade of histological malignancy. The longest survival from the onset of disease was 26 years; the shortest was 2 years.

All patients received radium therapy, 3 patients received supplemental x-ray therapy, and 5 were treated surgically.

The authors conclude that carcinoma confined to a Bartholin gland may be treated effectively by surgery, radium therapy and x-ray therapy in combination. In general, the prognosis of this type of lesion is fairly good if thorough early treatment is instituted.

(The fact that only 7 cases of primary carcinoma of Bartholin's gland have been encountered in 37 years in a very large clinic is ample evidence of the rarity of the lesion. In my own private practice I have seen only 2 cases, and only a comparatively small group have been studied in our Laboratory of Gynecological Pathology at the Johns Hopkins Hospital. Incidentally these are to be reported in the near future by Dr. L. H. Wharton, Jr. As the authors state, the malignancy in these cases is more often adenocarcinomatous than epidermoid in character, though the reverse was found to be true in the particular group re-

with a tumor within the abdominal wall. It closely resembled the recurrences seen in the 2 corporeal cancers.

In none of the cases was there any involvement of the inguinal glands below Poupart's ligament. It seems clear that the recurrence started somewhere along the course of the round ligament between the point at which the ligament left the peritoneal cavity and the point where it pierced the internal abdominal ring. It seemed possible that had a wider excision of the round ligaments been practised at the time of the initial operation, these recurrences might have been avoided.

(Such dissemination of corporeal carcinoma to the abdominal wall as the author describes in 2 cases is unusual, though it obviously can occur, and probably through the lymphatic route postulated by the author in these cases. For that matter, in the occasional case of corporeal cancer, the superficial inguinal glands may be involved, probably through the same route, since such involvement seems to occur chiefly when the endometrial cancer area is near the point of uterine insertion of the round ligaments. In the radical panhysterectomy as ordinarily performed for corporeal cancer, the round ligaments are commonly cut well out toward the pelvic wall, and whether the removal of an additional 2 or 3 inches, up to the internal ring, would lessen the hazard of such abdominal wall or inguinal recurrence, it is difficult to be sure, especially as the extraperitoneal portion of the ligament and the inguinal glands would still be left behind. The additional step described by the author, however, is a simple enough one, and certainly there can be no criticism of its performance, even though one may be skeptical about the degree of additional protection it affords.—Ed.)

EXCISION OF CYSTS OF BARTHOLIN'S GLAND

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Surg. Clin. North America, 29: 843, 1949

The incidence of cyst of Bartholin's gland seems to be decreasing with earlier and better treatment of genital infection. These cysts should be excised at a time of election, when the cyst is distended and when no infection is present. The incision for excision of the cyst is made directly over it in the longitudinal axis of the vulva, preferably on the cutaneous side. The cyst may be dissected up by sharp dissection with facility. Bleeding is profuse but can be controlled with fine hemostats which need not be ligated. After removal of the cyst, a continuous, fine chromic suture with an atraumatic needle is used to effect the closure. The single suture obliterates the depth of the wound and approximates the sides of the cavity by passing it back and forth 3 times. The same material is used for closure of the skin as a subcuticular structure. This type of closure results in a minimum of reaction in the wound and avoids hemorrhage.

(Excision of Bartholin gland cysts is a minor procedure, but it is not infrequently a rather pesky and vascular little operation. The region is a very vascular one, some of the blood

THE SURGICAL TREATMENT OF INTRACTABLE DYSMENORRHEA

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Mississippi Doctor, 27: 24, 1949

The author presents the technique and results of presacral neurectomy in 9 cases of intractable dysmenorrhea in which all other means of treatment had failed. Of the 9 patients, 5 have obtained complete relief, 2 have had partial relief, and 2 have had no relief.

Only patients with essential dysmenorrhea will be benefited by this operation. The cases to be treated should be selected on the basis of a complete cycle without ovulation as covered by the administration of diethylstilbestrol. If this period is painless, presacral neurectomy will relieve the dysmenorrhea. Presacral neurectomy will not relieve pain arising from the tubes and ovaries. Trial therapy by all other conservative means should be given before operation is performed.

(I was interested in the author's statement that the selection of cases for presacral neurectomy should be based on relief or non-relief of pain through the ovulation-inhibiting effects produced by diethylstilbestrol in the preovulatory phase. This plan will certainly prevent or greatly mitigate the pain of the succeeding period if the estrogen is started sufficiently early in the cycle. My own practice is to begin the dosage on the second day of the flow, i.e. the second day of the cycle, and keep it up for about two weeks. However, I question whether the test can be considered infallible, one reason being the not infrequent obstruction into the clinical picture of the psychogenic factor. I cheerfully endorse the last two sentences of the abstract.—Ed.)

OPERATIVE PROCEDURES FOR THE TREATMENT OF STERILITY
AND OVARIAN DYSFUNCTIONS

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Am. J. Obst. & Gynec., 57: 1069, 1949

The author reported upon decortication of the ovary in 1937. He realizes the dangers inherent in the use of this procedure for endocrine dysfunction. However, there are a certain number of cases which do not respond in any way to endocrine therapy. The author has operated upon only 11 cases during the past 11 years.

If the ovary is large, but not a neoplasm, a wedge of substance is removed in its longitudinal axis, the defect being closed with interrupted or figure-of-eight

ported. In the adenocarcinomatous variety there is apt to be little question of the Bartholin gland origin, when this is combined with the location of the lesion. There may be more doubt in the epidermoid group, in view of the fact that primary carcinoma of the vulva is practically always of epidermoid type, so that, except in the smaller lesions fairly well limited to the Bartholin gland area, one may not be justified in excluding an origin from the overlying vulvar surface. The prognosis is in general unfavorable, especially since most cases come under observation late, sometimes because in its early stages the lesion may be mistaken for a chronic inflammatory process. A combination of surgery and radiotherapy is most frequently indicated, and the surgery to be employed, in cases where there are no such contraindications as age and debility of the patient or a too advanced stage of the disease, should be of the same radical type as is employed for primary carcinoma of the vulva, preferably the Basset type of complete vulvectomy and gland excision.—Ed.)

PRESACRAL NEURECTOMY

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Surg. Clin. North America, 29: 861, 1949

In a study of 100 consecutive cases in which presacral neurectomy had been performed, Marshall and Kennedy reported 90% complete relief of all symptoms associated with menstruation in patients with primary dysmenorrhea and 80% in patients with secondary dysmenorrhea. Apparently division of the presacral nerve does not appreciably alter any normal physiology of the pelvic organs. It must be remembered that presacral neurectomy is symptomatic treatment and not a form of therapy dealing directly with the cause of the symptom.

Presacral neurectomy is performed under spinal anesthesia. A dilatation and curettage is done first. The abdomen is entered through a lower midline incision. A careful exploration is done and any corrective surgical procedures which may be indicated are performed. The intestine is packed off in such a way as to expose the promontory of the sacrum, the bifurcation of the aorta, and the iliac vessels. The posterior parietal peritoneum is divided in the midline from just above the bifurcation of the aorta down to the level of the bifurcation of the common iliacs. The peritoneum is retracted laterally. The triangle formed by the bifurcation of the aorta and the common iliac arteries is then well exposed. The left common iliac vein is seen medial to the corresponding artery. The right common iliac vein is not visualized. The right ureter is usually exposed, the left ureter rarely so. A tape is passed about the plexus, lifting it from its bed. With meticulous dissection, all of the fibers of the plexus and the closely adjacent connective tissue are excised from a level 2 to 3 cm. above the bifurcation of the aorta to the bifurcation of the common iliacs. The distal and proximal stumps are ligated. An appendectomy is usually performed.

(See comment on two following abstracts.—Ed.)

obstruction. I am sure that every experienced gynecologist will agree that many tinkering operations of this type, sometimes done for no valid indication, are shown by secondary operations to have done the patient far more harm than good.

To repeat, I would have the impression, from the few published reports rather than from my own experience, that excision of parts of the ovary probably is helpful in a very limited group, but the exact indications are not always clear, nor is the rationale of this procedure. One can readily imagine the havoc which might follow from the indiscriminate application of such a surgical plan in the treatment of endocrinopathic amenorrhea.—Ed.)

THE VALUE OF THE UTEROSACRAL LIGAMENTS IN UTERINE DISPLACEMENTS

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J. M. A. Georgia, 38: 199, 1949

The uterosacral ligaments are flat, fibromuscular bands which pass backward from the upper part of the cervix, at the level of the isthmus, around the rectum to the first sacral vertebra opposite the lower border of the sacro-iliac joint. They are stationary supports to the uterus and hold the cervix in the posterior part of the pelvis. With weak uterosacral ligaments and anterior displacement of the cervix, the fundus falls back, permitting the intra-abdominal pressure to aggravate the displacement.

Mere shortening of the round ligaments will often fail to maintain the uterus in its normal position. In the surgical treatment of pathological retroversion, the authors routinely identify and shorten the uterosacral ligaments. The ligaments are sewed together with a continuous suture of #2 braided silk. If the ligaments consist merely of peritoneal folds, new ligaments are constructed by first scarifying the folds and then using a running suture of #2 braided black silk on either side. When these are tied, a bunched ligament is obtained on each side which can be further shortened if necessary, by suturing the ligaments together. Ureteral injury and constriction of the bowel should be avoided.

A similar shortening of the uterosacral ligaments may be of value at the time of total hysterectomy as prophylaxis against subsequent vaginal vault prolapse.

(This is a paper I was mighty glad to see, because it stresses a point which is important and which is commonly overlooked in the performance of hysteropexies. As a matter of fact, I had for some time been thinking of writing a paper on the subject myself, so that the expungement of this incentive by the present paper may be credited to its virtues and accomplishments. As the authors say, a mere shortening of the round ligaments accomplishes very little in the frequent cases of either retroversion or retroflexion in which the cervix has, so to speak, broken away from its posterior moorings, poking its nose downward and forward along the axis of the vagina, so that the palpating finger often encounters it within a couple of inches of the vaginal orifice. No matter how much the round ligaments are shortened, the downward and forward sag of the cervix will still persist unless the elongation of

sutures of plain catgut. In most of the cases the operation consisted of denuding a portion of the cortex, and controlling small bleeding points.

In the 11 cases whose ovaries were operated upon, 10 had rare or absent menstruation. The remaining patient had excessive flow. Two of the patients had theca cell tumors which were removed. With one exception, the remainder of the patients were benefited by partial excision of the ovarian cortex, using a wedge resection when the ovaries were unusually large. Suspension of the ovaries was freely used. Five of these patients have become pregnant.

The author presents 20 cases in which major operative intervention seemed justified for the correction of sterility. Eight of these had cystic ovaries. In these cases the involved ovary was removed and the tube salvaged and suspended so as to increase the chances of an ovum being received in the fimbriated extremity. Three had myomectomy performed, with good results; 4 had various operations for closed or absent tubes, all without results. The remaining 5 were treated by uterine suspension. Of the 20 cases, 14 have now become pregnant, and to date, have delivered 22 full-term living infants.

(The hazard in publishing a paper of this sort is that the operative procedure which is advocated is quite sure to be applied indiscriminately by some in the treatment of amenorrhea. While I am sure that the author would not wish this, I do not believe that he himself has stressed sufficiently the limitations of the application to a certain small group of cases, as does Stein (*Am. J. Obst. & Gynec.*, 50: 385, 1945) in his description of an essentially similar procedure. The fact that in 2 of Reycraft's 11 cases a thecoma was present, and that another of his patients had what was apparently a Chiari syndrome, does not speak well for the selectiveness of the group.

It would be naive to consider that ovarian dysfunction is a simple plus or minus affair, as thyroid dysfunction almost seems to be. Just because resection of thyroid tissue cures hyperthyroidism and thyroid administration is so useful in thyroid deficiency, one cannot assume that similar rules apply to the ovary, and they most certainly do not. As a matter of fact, the procedure recommended by both Stein and Reycraft is a somewhat paradoxical one in that ovarian tissue is removed when ovarian function is already deficient. Many years ago the superficially more rational procedure of resecting ovarian tissue was recommended in cases of assumed ovarian hyperfunction manifested by functional bleeding, though the failure of this plan soon led to its abandonment.

The fallaciousness of such simple quantitative assumptions as have been mentioned is explained by the intricacy of the reproductive hormonal cycle, and especially of the hypophyseo-ovarian interrelationships. Without meaning to express any great enthusiasm for the general plan, I believe that reduction in the amount of ovarian tissue is helpful in a small proportion of cases of amenorrhea and sterility, including those described by Stein as often associated with obesity and some degree of hirsutism, but I also believe that any such benefit comes for other reasons than these authors suggest. As far back as 1928 Lipschütz enunciated his "law of follicle constancy," establishing that ovarian resection causes a concentration of the continuing gonadotrophic function of the hypophysis upon a reduced ovarian surface, thereby increasing follicle maturation and estrogen production. As a matter of fact, I believe that this very mechanism is responsible for many of the cases of advanced cystic degeneration in which the conservative surgeon leaves portions of ovary with the laudable purpose of retaining ovarian function.

One can certainly not accept unqualifiedly the old dictum of "Either take out an ovary completely or leave it alone," but it carries with it a considerable measure of truth. Resection of ovaries, no matter how neatly done, carries with it a hazard of intestinal adhesions, and if done clumsily, these adhesions may be extensive and lead to angulation and

hysterectomy with colporrhaphy, 6 by vaginal colporrhaphy with shortening of the cardinal ligaments, 10 by colectomy—6 subtotal and 4 total.

Subtotal colectomies were modified from the LeFort operation only in that a perineorrhaphy was performed. Total colectomies were performed by first doing a vaginal hysterectomy, Mayo technique. There were no deaths and no complications with any of the colectomies.

(Colectomy of the LeFort type, or some modification thereof, is a procedure of accepted and undoubted value in women in whom, by virtue usually of age, marital life is no longer considered important. But gynecologists, and certainly patients, will differ widely in their ideas as to any sort of age demarcation. Patients and their husbands should have a deciding vote when such a procedure is contemplated. I used to know an old colored fellow who made the sad but profound observation, "You know, Doc, after 60, sin jes' gradually leaves a fellow." On the other hand, who has not been consulted by women much older than this, no doubt on the sinister goading of their husbands, because of dyspareunia. I remember an old gal of 67 who had had a plastic procedure done, with overapproximation of the tissues and resulting inability to have coitus. Her sufferings were so pitiable that I thought it best to widen the canal with a colpoplastic procedure. After healing was complete I playfully suggested that she and her 69 year old husband go off on a second honeymoon and let me know how things went. A short time later I was surprised to receive from Atlantic City a telegram which read "Everything lovely."

Valuable as the LeFort operation is in certain cases, it carries with it a definite finality and must be regarded as of defeatist type. Personally I believe it is often done when a genuinely corrective procedure, such as a vaginal hysterectomy or a Manchester type of operation, can be done just as readily and safely and almost as quickly, under local anesthesia even in old women. Holding these views, I am sure that I perform a smaller proportion of LeFort operations than do many other gynecologists, although I appreciate fully that in a small proportion it should be the method of choice.—Ed.)

A SIMPLE METHOD OF APPLYING VAGINAL RADIUM

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Texas State J. Med., 45: 209, 1949

Vaginal radium is usually applied by means of a colpostat held in place with vaginal packing. This method has several disadvantages: (1) the packing must be changed frequently, (2) packing interferes with voiding and defecation and douching, (3) the pack becomes malodorous, (4) the colpostat often becomes misplaced and may cause an irradiation proctitis and cystitis, (5) the patient must be confined to bed during treatment, and (6) the packing may cause the patient discomfort.

Many of these disadvantages can be avoided by the use of a Gellhorn type of pessary drilled to accommodate the radium containers. The entire course of irradiation can be delivered at one time.

the uterosacral ligaments which makes it possible is corrected by some form of plication. Simple side-to-side approximation of these ligaments is often not sufficient and various techniques of plication may be employed. I myself often use a figure-of-8 type of plicating suture, which should include also the posterior surface of the cervix in order to avoid leaving a slot into which an intestinal loop might slip. It is hardly necessary to emphasize that the plicating suture should not be introduced in too wide, deep and flourishing a fashion, as the ureter might be included in its sweep.

I do not agree with the authors that such uterosacral plication is a necessary routine in every suspension for the simple reason that the uterosacral ligaments are not always elongated, although it is certainly true that suspension operations of any kind are rarely indicated *per se* for displacements of this sort. Often, however, as in conservative operations for endometriosis, it is desirable to draw the uterus anteriorly from the rectum by shortening the round ligaments, and in such cases the uterosacral ligaments are often short and sometimes thickened and infiltrated. The conservative attitude of modern gynecologists toward uncomplicated retrodisplacements has tremendously lessened the field for primary suspension operations, although they are still justified in a limited group, while some form of usually round ligament suspension is often a valuable addendum to an operation performed for some other indication.

By the same token, uterosacral plication is often a valuable addition to the technique of hysterectomy of either the *total* or *subtotal* variety. *This point has been stressed by a number of writers, and especially by Lillian Farrar.* In multiparous women especially the ligaments are often greatly elongated, and the technique of suspending the vaginal vault or cervical stump should include a shortening of the uterosacral ligaments. I am convinced that this procedure greatly diminishes the hazard of subsequent prolapse of the vaginal vault or cervical stump.

While the thesis of the authors of the present paper is not a new one, they deserve credit for reemphasizing its importance.—Ed.)

COLPECTOMY—IN THE MANAGEMENT OF PROLAPSE OF THE UTERUS AND VAGINA

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J. Maine M. A., 40: 75, 1949

Review of the literature shows that colpectomies have a very useful place in surgery. All authors agree that subtotal colpectomy is very safe and can be done easily under local infiltration anesthesia. However, the cervix, the corpus uteri, and the adnexa must be free from pathology.

In 1,023 gynecological operations, there were 206 cases of second and third degree procidentia; 190 of these cases had prolapsed uteri and 16 cases had prolapsed cervixes. There were 103 cases of first degree prolapse. The large majority of the women with second and third degree prolapse were 50 years or older. The 103 cases of first degree prolapse were treated by vaginal repairs, cauterizations and conization as indicated. Of the 216 cases of procidentia, 122 were treated by vaginal hysterectomy with colporrhaphy, 78 by abdominal

SUBJECT INDEX

VOLUME 4, 1949

ABDOMEN

- acute, caused by corpus luteum rupture in pregnancy during coitus, followed by abortion, 58
- chorionepithelioma, unsuspected abdominal, 551
- intra-abdominal hemorrhage from ectopic pregnancy, variant of Hofstatter-Cullen sign, 790

ABORTION

- as cause of death, 221
- attempted, with potassium permanganate douche, death from, 826
- corpus luteum rupture during coitus causing acute abdomen followed by, 58
- criminal, and intestinal destruction, 827
- criminal instrumental, dangers, 398
- habitual, 624
- missed, evaluation of conservative management, 485
- new classification and nomenclature for newborns, including prematures and abortions, 212
- trauma and interruption of pregnancy, 368 *therapeutic:*
- 674
- cardiac indication, 672, 794
- nephritis and diabetes, 676
- psychiatric indications, 675
- pulmonary tuberculosis, 674
- Roman Catholic views, 673
- uterovesical fistula following, new operation, 428

ADDISON'S DISEASE

- pregnancy, 800

ADENOMYOSIS

- corpus, with fibroadenoma of cervix, 854
- uterus, with tuberculous infection, 282

ADOLESCENCE

- girl, 733

ADRENAL GLANDS

- adreno-genital syndrome, note on antiquity, 834
- cortical functions in grafted mouse ovaries, 93
- feminizing tumor causing gynecomastia in 5-year-old boy; virilizing tumor in 5-year-old girl, 88
- sex hormone secretion by cortical tumors in mice, 681

AMBULATION

- early, in obstetrics and gynecology, 483

AMENORRHEA, *See* MENSTRUATION, disorders.

AMNION

- use in construction of artificial vagina, 433

AMNIOTIC FLUID

- embolism, 62
- pulmonary embolism, report of fatal case and review of literature, 503
- water and sodium of; rate of renewal in woman, as determined by tracer techniques, 176

ANATOMY

- reasons for caudal anesthesia failure, 482
- surgical, of cystocele and urethrocele with reference to pubocervical fascia, 875

ANEMIA, *See* BLOOD, diseases.

ANESTHESIA

- caudal, anatomic reasons for failure, 482
- caudal and spinal, continuous, present status, 339
- caudal, combined procaine-pontocaine single injection technic, 820
- caudal, continuous, 33
- caudal, continuous, shock during, 30
- cesarean section, 823
- cyclopropane in cesarean section, 72
- intravenous demerol-scopolamine amnesia, 481
- obstetrical, at Cedars of Lebanon Hospital, 10-year study, 824
- peridural and caudal, continuous, in obstetrics, 821
- peridural, cold pressor test as criterion for selection, 228
- premedication and; current practices at Boston Lying-In Hospital, 341
- regional nerve block, treatment of eclampsia, 350
- spinal, fatalities, 31
- spinal, for cesarean section, 72
- spinal, high; mechanism of fall in arterial pressure produced in patients with essential hypertension, 227
- spinal, physiologic study of hypertension in pregnancy toxemia, 607

MISCELLANEOUS

HEMATOMA OF THE RECTUS ABDOMINIS MUSCLE SIMULATING GYNECOLOGICAL DISEASE

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J. Mount Sinai Hosp., 6: 280, 1949

Idiopathic or non-traumatic hemorrhage into the rectus abdominis sheath occurs more frequently in women than in men and is most often mistakenly diagnosed as an ovarian tumor. The authors report 2 cases of idiopathic hematoma of the rectus sheath, incorrectly diagnosed as ovarian tumors. Evacuation of the extravasated blood produced a clinical cure in both cases.

The syndrome occurs more frequently in elderly patients and is often antedated by paroxysmal coughing. It is usually confused with ovarian tumors. Ecchymosis of the abdominal wall is a late sign and rarely of aid in diagnosis. A mortality varying from 4 to 15% is reported in the literature. The treatment advocated is early surgical intervention.

(The hemorrhage into the rectus sheath which the authors describe is not infrequently associated with rupture of rectus muscle fibers, and, as they state, is generally due to sudden and unguarded muscle effort, especially coughing. In a preceding generation this condition was often spoken of as Zenker's disease, although I have not come across this designation in the literature of recent years. As the authors say, the clinical picture presented by these patients is apt to be confused with that of intraabdominal disease, because of the extreme pain and tenderness and the board-like rigidity commonly associated. These are likely to be in the median or paramedian area, so that acute appendicitis is not often simulated, especially as nausea, vomiting and distention are most often absent. Fortunately the condition is a rare one, but I was rather surprised to read that the authors have found the mortality rate to be from four to fifteen per cent, especially as the operative treatment is usually comparatively simple.—Ed.)

- groups:*
- Coombs test in detection of iso-sensitization of newborn, 217
 - erythroblastosis associated with Rh-positive mothers, 67
 - interpretation of Rh antibodies, 215
 - medicolegal aspects of Rh-Hr Types, 818
- BLOOD PRESSURE**
- changes in eclampsia, electroencephalographic records in relation to, 40
 - effect of low sodium diet and rice diet on arterial pressure, 638
 - effect of veratrum viride in normal and toxemic pregnancy, 793
 - maintenance in normal and toxemic pregnancy, evaluation of neurogenic and humoral factors using tetra-ethyl-ammonium chloride, 362
 - mechanism of fall in arterial pressure produced by high spinal anesthesia in patients with essential hypertension, 227
 - minimal sodium diet, effect on ambulatory hypertensives, 189
- BLOOD VESSELS**
- vascular architecture of rat uterus as influenced by estrogen and progesterone, 401
 - vascular changes of skin in pregnancy, vascular spiders and palmar erythema, 777
 - vascular congestion and hyperemia, effect on structure and function of female reproductive system, 593
 - vascular patterns in human ovary, 710
- BONE**
- osteitis pubis following ureterolithotomy, 722
 - prevalence and distribution of ossification centers in newborn, 661
- BRAIN**
- cerebral blood flow and metabolism in normal and toxemic pregnancy, 363
 - cerebral complications resulting from hypertension caused by vasopressor drugs in obstetrics, 789
- BREAST**
- carcinoma, advanced, testosterone propionate in treatment, 830
 - carcinoma, aging processes in ovaries of mice of strains differing in incidence of, 711
 - carcinoma, comparative statistical study, 456
 - chronic cystic mastitis and cancer, premenstrual tension and menstrual anomalies, similarity of estrogenic effect in, 245
 - fibro-adenosis, effect of endocrines, 683
 - is chronic cystic mastitis a precancerous lesion?, 312
 - stilbestrol in late malignant disease, 246
- BROMSULFALEIN**
- liver function in newborn, 662
- CANNULA**
- inflatable, for cervical obturation in tubal insufflation and hysterosalpingography, 729
- CARCINOMA**
- advanced, complete excision of pelvic viscera: one-stage abdominoperineal operation with end colostomy and bilateral ureteral implantation into colon above colostomy, 430
 - atypical endometrial hyperplasia simulating adenocarcinoma, 127
 - Bartholin's gland, primary, 106
 - Bartholin's glands, radium therapy, 881
 - breast, advanced, testosterone propionate in treatment, 830
 - breast, aging processes in ovaries of mice of strains differing in incidence of, 711
 - breast, chronic cystic mastitis, premenstrual tension and menstrual anomalies, similarity of estrogenic effect in, 245
 - breast, comparative statistical study, 456
 - breast, stilbestrol in late malignant disease, 246
 - carcinogenic and anticarcinogenic substances, 595
 - cervix, comparison of accuracy in diagnosis of vaginal smear and biopsy, 123
 - cervix, complicating procidentia uteri, 126
 - cervix, cytology as early diagnostic method, 414
 - cervix, 5-year end results of irradiation therapy at Memorial Hospital, 420
 - cervix, *in situ*, smear diagnosis, 118
 - cervix, modern concepts, 315
 - cervix, necropsy findings, implications for treatment, 702
 - cervix, preclinical diagnosis, use of cervical cone knife in patients with positive vaginal smear, 417
 - cervix, preinvasive, 701
 - cervix, radical operation for, 418
 - cervix, rectal injuries following radium treatment, 259

ANGINA

- of effort, in pregnancy, 195

ANOMALIES

- complete congenital absence of vagina with bilateral herniae of uterus, tubes and ovaries, 410
- ovarian agenesis, case report with post-mortem findings, 716
- ovary, 159
- pelvic ectopic kidney, complicating pregnancy and labor, review of literature, 737
- ruptured horn of bicornate uterus, 557
- septate uterus, double vagina and other congenital abnormalities with pregnancy, 200
- solitary pelvic kidney with vaginal aplasia, 874
- uterus bicornuis unicollis, carcinoma in one horn, 857

ANTICARCINOGENS, *See* CARCINOMA.ANTI-HORMONES, *See* HORMONES.

ANURIA

- and oliguria in pregnancy toxemia, 634

APPENDIX

- acute and chronic appendicitis in pregnancy, comparative study, 797
- ruptured, with generalized peritonitis, in term pregnancy, 502

ARTIFICIAL INSEMINATION

- position in treatment of sterility, 441
- timed by rat ovulation test, 450
- tubal, in certain types of sterility, 591

ASCITES

- pseudomucinous ovarian cyst with hydrothorax and, 139

ASPHYXIA

- neonatorum, and the vernix membrane, 808

ATABRINE

- treatment of *Trichomonas vaginitis*, 258

ATRESIA

- partial, of vagina, 255

AUREOMYCIN

- treatment of lymphogranuloma venereum and granuloma inguinale, 633

BACTERIOLOGY

- Fallopian tubes removed at operation, 562
- flora of postpartum uterus, effect of penicillin therapy, 806
- vagina in 75 normal young adults, 847

BARTHOLIN'S GLAND

- carcinoma, primary, 106

- carcinoma, radium therapy, 881

- cysts, excision, 880

BENZODIOXANE

- physiologic study of hypertension in pregnancy toxemia, 609

BIOPSY

- diagnosis of cervical carcinoma, comparison of accuracy of vaginal smear and, 123

BIRTH PRIMACY

- idiopathic epilepsy, 66

BLADDER

- complete exstrophy, management of labor, 64
- contracture of vesical neck, 142
- cystocele, surgical anatomy, with reference to pubocervical fascia, 875
- evacuation following gynecologic operations, efficacy of certain drugs in promoting, 721
- vesicovaginal fistula, 102
- vesicovaginal fistula following radium treatment for cervical carcinoma, treatment, 295

BLOOD

- cerebral flow and metabolism in normal and toxemic pregnancy, 363
 - erythrocyte sedimentation velocity in normal pregnancy, 178
 - gonadotrophins in pregnancy in relation to fetal sex, 27
 - measurement of venous flow in legs of women at term and in puerperium, using radioactive sodium, 476
 - plasma volume and extravascular fluid volume in pregnancy and puerperium, 471
 - soybean trypsin inhibitor preventing toxic effects of human placental thromboplastin, 487
 - transfusion, replacement, for erythroblastosis, via umbilical vein, 214, 218
 - transfusions, massive, in management of ruptured uterus and obstetric shock, 801
 - urea, effect of pyridoxine, 639
- diseases:
- anemia simulating pre-eclamptic toxemia, 489
 - erythroblastosis: *see* Erythroblastosis.
 - hyperlipemia, severe, in nondiabetic pregnancy, 643
 - sickle cell anemia and pregnancy, 798
 - sickle cell trait: incidence and influence in colored gravidae, 377

- in Dublin, 669
- modern indications, 389
- postmortem, after death from bulbar poliomyelitis, 664
- sarcomatous degeneration of myoma found at, 421
- spinal anesthesia, 72
- sulfadiazine and penicillin prophylaxis, 230
- supravescical extraperitoneal, choice for infected patient, 671
- survey in Minneapolis, Minnesota, 1946, 224

CHLOROMYCETIN

- granuloma inguinale, therapy, 851

CHOREA

- choreiform behavior in pregnancy, 56

CHORIONEPITHELIOMA

- clinical pathological conference, case report, 277
- hydatidiform mole and, 192
- primary teratomatous, of ovary, 288
- stilbestrol treatment, 194
- unsuspected abdominal, 551
- unusual types, 553
- uterine cervix, 552

CIGARETTE, *See TOBACCO.*

COAGULATION

- coagulability of menstrual fluid, 408

COITUS

- corpus luteum rupture in pregnancy during, followed by abortion, 58
- false vagina formed by, 845
- rupture of vaginal vault during, 256
- vaginal injury at, 256

COLD PRESSOR TEST

- as criterion for selection of peridural anesthesia, 228

COLITIS

- chronic ulcerative, and pregnancy, 53

COLPECTOMY

- management of prolapse of uterus and vagina, 886

CONCEPTION

- number of sperms required for fertilization, 441
- physiology, 774
- rat test prediction of day of ovulation, 96

CONE KNIFE

- cervical, use in patients with positive vaginal smear in diagnosis of preclinical cervical cancer, 417

CONIZATION

- wide cervical, 580

CONNECTICUT

- incidence and survival picture in cancer among females, 1935-1946, 115

CONTRACEPTION

- efficacy of suppository and of jelly alone, 399
- Grafenberg's ring, complications following intrauterine insertion, 455

CONTRACTED PELVIS, *See PELVIS.*

CONTRAST MEDIUM

- water-soluble, in hysterosalpingography, 305

COOMBS TEST

- detection of iso-sensitization of newborn, 217

CORPUS LUTEUM

- pregnancy, rupture during coitus, causing acute abdomen followed by abortion, 58

CREDÉ'S MANEUVER, 210

CULTURE

- Döderlein's bacillus, technique for isolation, maintenance and, 534
- trichomonad infestations, method for diagnosis, 692

CYCLOPROPANE, *See ANESTHESIA.*

CYSTOCELE, *See BLADDER.*

CYSTS, *See under regions and organs.*

CYTOLOGY, *See Vaginal Smear.*

DECIDUA

- acute decidual endometritis and metritis, 543
- bleeding in pregnancy, 204

DEMEROL, *See ANESTHESIA.*

DESOXYCORTICOSTERONE ACETATE

- and nephrotoxic rabbit anti-rat placenta serum injected in pregnant rat, 488

DEUTERIUM OXIDE

- permeability of human placenta to water and supply of water to fetus as determined with, 175

DIABETES MELLITUS

- fertility, maternal mortality and fetal loss rate, 493
- infant birthweight, relation to subsequent maternal diabetes, 50
- investigation on pregnancy in diabetic animals, 205
- prediabetic pregnancy, 374
- pregnancy, 495
- termination of pregnancy in nephritis and, 676

- cervix, repair of vesicovaginal fistula following radium treatment, 295
 - cervix, retreatment, 549
 - cervix, retroperitoneal lymph node dissection, 878
 - cervix, role of surgery in treatment, 575
 - cervix, therapeutic problem, 856
 - cervix, total versus subtotal hysterectomy, 435
 - cervix, treatment, 266
 - cervix, treatment in local tumor clinics, 550
 - cervix, unsuspected, in gynecological patients, 700
 - cervix, urinary tract changes, 873
 - chronic cystic mastitis a precancerous lesion?, 10-year follow-up of 26 cases, 312
 - corporeal and ovarian, excision of round ligaments, 879
 - corpus, and fibroid, treated with radium and hysterectomy, 268
 - corpus, in one horn of uterus bicornuis unicollis, 857
 - corpus, radiation treatment, 264
 - early diagnosis by study of exfoliated cells, 415
 - endometrial, adjunctive radiotherapy in surgical treatment, 131
 - estrogens carcinogenic in human female?, 406
 - Fallopian tube, primary, 6 cases, 284
 - female generative organs, 117
 - female genital tract, direct current measurement as aid to detection, 546
 - fundus in rabbit, evolution of, 280
 - fundus, treatment, 124
 - genital, 252, 454
 - genital, diagnosis by vaginal smear, 113, 119, 120, 698
 - granuloma inguinale of cervix diagnosed as, 554
 - gynecologic aspect, 116
 - hyperplasia and, 550
 - incidence and survival picture in Connecticut females, 115
 - ovary, papillary cystadenocarcinoma treated with large doses of testosterone propionate, 717
 - ovary, pseudomucinous cystadenocarcinoma, 292
 - pelvic, advanced, radical surgery, 699
 - pelvic, intestinal changes secondary to irradiation, 130
 - pelvic, observations on delay period in diagnosis, 547
 - recurrent and uncontrolled, after previous irradiation and conservative surgery; surgical problem, 877
 - Strang Cancer Prevention Clinics, 113
 - tuberculosis of cervix macroscopically resembling cervical carcinoma, 267
 - urethra, radium therapy, 720
 - urethra, relationship of urethral caruncle, 140
 - uterus, adenocarcinoma, histologic findings following intracavitary radiation, 723
 - uterus, and vagina, vaginal hysterectomy for, 296
 - uterus, application of silver carbonate stain for diagnosis by vaginal smear, 120
 - uterus, cervical smear in diagnosis, 544
 - uterus, colpocytological method of diagnosis, 122
 - uterus, cytologic diagnosis, 546, 697
 - uterus, early diagnosis, 112
 - uterus, early diagnosis by simple screening methods, 121
 - uterus, Papanicolaou test in early diagnosis, 416
 - vaginal, in 14-year-old girl, treated by radiation, 532
 - vulva, 103
 - vulva, adenocarcinoma, cylindroma type, 693
 - vulva, and cervical, treatment, 105
 - vulvo-perineal epithelioma and lymphogranulomatosis, 530
- CARUNCLE
- urethral, relationship to urethral carcinoma, 140
- CAUDAL ANALGESIA, *See* ANESTHESIA.
- CEPHALOMETRY, *See* RADIOGRAPHY.
- CERVIX, *See* UTERUS, *cervix*.
- CESAREAN SECTION
- abdominal pregnancy following scar rupture, 499
 - anesthesia, 823
 - cyclopropane, 225
 - extraperitoneal, in profoundly infected patient, 668
 - fetal mortality and morbidity, 391
 - hysterectomy at Chicago Lying-In Hospital, 69

ERYTHROCYTE

- sedimentation velocity in normal pregnancy, 178

ESTROGENS

- carcinogenic in human female?, 406
- cream in treatment of senile vaginitis, 692
- diethylstilbestrol and testosterone propionate administered in early pregnancy, response of fetal reproductive system, 87
- diethylstilbestrol, effect on urinary excretion of pregnanediol and endogenous estrogens in pregnancy, 781
- diethylstilbestrol, effects of prolonged therapy on endometrium, 686
- diethylstilbestrol in late malignant disease of breast, 246
- diethylstilbestrol in prevention and treatment of complications of pregnancy, 190
- diethylstilbestrol treatment of chorion-epithelioma, 194
- diuretic effects in last 4 months of pregnancy, 185
- estradiol benzoate in oil solution and aqueous suspension of crystals, mode of action in castrated female, 521
- estradiol, mechanism of inactivation by rat liver in vitro, 246
- estradiol pellet implantation in treatment of menopause, 844
- estrone and progesterone, precipitate, for induction of bleeding in amenorrhea, 95
- homologous ovarian and testicular tumors producing, 864
- hyperestrogenism treated with lactogenic hormone, 243
- inactivation by women with vitamin B deficiency, 240
- indiscriminate use in menopause, 404
- meprane in treatment of menopausal syndrome, 97
- ovarian insufficiency, mechanism of action in, 518
- pellets, intravaginal implantation, stimulation of ovarian function and induction of pregnancy, 832
- premenstrual tension, menstrual anomalies, chronic cystic mastitis and cancer of breast, similarity of estrogenic effect in, 245
- urinary excretion of 17-ketosteroids and, in metropathia hemorrhagica, 403

- vaginal mucosa, effects of various preparations, 84
- vaginal smear in assay of oral or intramuscular estrogens, 247
- vascular architecture of rat uterus as influenced by progesterone and, 401

EXERCISE

- progressive resistance, in functional restoration of perineal muscles, 154

EYE

- lens changes of embryo after rubella, 659
- ocular manifestations of pregnancy, 637
- retrolental fibroplasia in premature infants, 656

FACE PRESENTATION, *See LABOR, presentation.*

FALLOPIAN TUBES

- bacteriology of tubes removed at operation, 562
- bilateral herniae of uterus, ovaries and, with complete congenital absence of vagina, 410
- blocked, pressure treatment, 439
- carcinoma, primary, 6 cases, 284
- fibromyoma, 235
- hydatidiform mole, 286
- hysterosalpingography, 592
- hysterosalpingography, advantages under fluoroscopic control, 443
- insufflation and hysterosalpingography, cervical obturation with inflatable cannula, 729
- insufflations, 592
- interstitial pregnancy following homolateral salpingectomy, 301
- patency tests, 439
- persufflation curve in myxedema, effect of thyroid therapy, 682
- pneumo-pyosalpinx, 568
- tertiary syphilis of uterus and adnexa, 597
- torsion of hydrosalpinx in pregnancy, 199
- torsion of normal tube complicating pregnancy, 497
- tubal insemination in certain types of sterility, 591
- twisted hematosalpinx, 709
- unilateral hydrosalpinx with torsion without involvement of ovary, 287

FAT GLOBULES TEST

- diagnosis of ruptured fetal membranes, 348

FERTILITY

- dysgerminoma ovarii, 426

DIBENAMINE

- physiologic study of hypertension in pregnancy toxemia, 609

DIBROMESTRONE

- radioactive, tissue localization and excretion routes, 90

DICUMAROL

- danger of treatment in pregnancy, 641

DIET, See NUTRITION.**DIURESIS**

- efficacy of certain drugs following gynecologic operations, 721
- estrogens in last 4 months of pregnancy, effects, 185
- sodium excretion in gravidæ, effectiveness of various agents, 42

DIVERTICULUM

- urethral, 570

DÖDERLEIN'S BACILLUS

- technique for isolation, maintenance and culture, 534

DUBLIN

- cesarean section, 669

DYSMENORRHEA, See MENSTRUATION, disorders.**DYSTOCIA, See LABOR, complications.****ECLAMPSIA**

- does eclamptogenic toxemia cause chronic hypertension?, 184
- electroencephalographic records in relation to blood pressure changes in, 40
- etiology, evaluation of recent theories, 359
- follow-up study, 44
- physiopathology, 188
- regional nerve block in treatment, 350
- severe preeclampsia, treatment, 36

ECTOPIC PREGNANCY

- 625
- abdominal, 628
- abdominal, following rupture of cesarean scar, 499
- bilateral tubal, 53
- interstitial, following homolateral salpingectomy, 4 cases, 301
- ovarian, 712, 713, 791
- primary abdominal, in lesser peritoneal cavity, 51
- unruptured primary ovarian, 293
- variant of Hofstatter-Cullen sign in intra-abdominal hemorrhage from, 790

ELDERLY PATIENT

- gynecologic surgery, risks and results, 143, 144

ELECTRODYNAMICS

- technique to aid detection of malignancy in female genital tract, 546

ELECTROENCEPHALOGRAM

- records in relation to blood pressure changes in eclampsia, 40

EMBOLISM

- amniotic fluid, 62
- pulmonary, by amniotic fluid, report of fatal case and review of literature, 503

EMBRYO

- lens changes after rubella, 659

EMBRYOLOGY

- development of levator ani muscle, 155
- mesonephric remnants in cervix, 704

ENDOCRINE GLANDS

- endocrine factors in female sterility, diagnosis and treatment, 447
- imbalance, development of leiomyomas in rats with, 684

ENDOMETRIOSIS

- 272
- causing small bowel obstruction, 3 cases, 274
- cervix, primary, 860
- clinical review, 858
- conservative management, 705
- conservative surgery, results in 138 cases, 706
- experimental, 109
- ileal obstruction caused by, 538
- ovarian adenofibroma with partial differentiation to, 718
- stromal, 540, 541
- surgical treatment, 861
- syncytial, syncytioma, 110
- treatment, evaluation, 275
- vaginal, following vaginal hysterectomy, 533

ENDOMETRIUM, See UTERUS.**EPILEPSY**

- idiopathic, and birth primacy, 66

ERGONOVINE

- control of hemorrhage attending delivery, comparison of intravenous oxytocin and, 349

ERYTHROBLASTOSIS

- associated with Rh-positive mothers, 67
- criteria of severity of hemolytic disease, 653
- replacement transfusion via umbilical vein, 214, 218
- reproductive histories of mothers of 322 erythroblastotic infants, 650

- congenital disease, antepartum diagnosis, 649
- disease, complicating pregnancy, indications for therapeutic abortion or avoidance of conception, 794
- tones, fetal, characteristic changes, 473

HEMATOMA

- rectus abdominis muscle, simulating gynecological disease, 888

HEMATOSALPINX, See FALLOPIAN TUBES.**HEMORRHAGE**

- abnormal uterine, 559
- abnormal uterine, arrest with pitressin tannate in oil, 92
- attending delivery, comparison of intravenous oxytocin and ergonovine in control of, 349
- decidual, in pregnancy, 204
- functional uterine, histology of endometrium, 535
- functional uterine, progesterone therapy, 679
- intra-abdominal, from ectopic pregnancy, variant of Hofstatter-Cullen sign, 790
- metropathia, urinary excretion of estrogenic substances and 17-ketosteroids, 403
- postpartum, and retained placenta, 804
- primary postpartum, 383
- retinal, hyperemesis gravidarum with, 486
- uterine, 112
- uterine, and ovarian tumors, 715
- uterine, induction in amenorrhea with precipitate estrone and progesterone, 95

HERMAPHRODITE

- interstitial tissue of, 91
- pseudo-, in twins, 731

HERNIA

- bilateral, of uterus, tubes and ovaries, with complete congenital absence of vagina, 410
- intestinal strangulation in pouch of Douglas, procidentia complicated by, 279

HISTOLOGY

- endometrium in functional hemorrhage, 535
 - findings following intracavitary radiation for uterine adenocarcinoma, 723
 - structural components of vagina, reconstructive surgery, 691
- HOFSTATTER-CULLEN SIGN**
- variant in intra-abdominal hemorrhage from ectopic pregnancy, 790

HORMONES (See also under specific hormones.)

- adreno-genital syndrome, note on antiquity, 834
- antihormone formation during gonadotrophic hormone therapy, 86, 831
- control of menstrual cycle, application of physiologic concepts to therapy, 837
- control of ovarian activity, 248
- effect on fibro-adenosis, 683
- endocrine factors in female sterility, diagnosis and treatment, 447
- endocrine imbalance, development of leiomyomas in rats with, 684
- factors involved in regulation of basal temperature in menstrual cycle and pregnancy, 100
- lactogenic (prolactin) treatment of hyperestrogenism, 243
- pellets, indications in therapy of endocrine and gynecic disorders, 520
- radioactive dibromestronone, tissue localization and excretion, 90
- sex, role in differentiation of sexes and sexual abnormality, 85
- sex, secretion by adrenal cortical tumors in mice, 681
- use and misuse in obstetrics and gynecology, 241

HOSPITALS

- cancer of cervix, 5-year end results of irradiation therapy at Memorial Hospital, 420
- cesarean hysterectomy at Chicago Lying-In Hospital, 69
- maternal mortality during 1937-1946 at Cincinnati General Hospital, 396
- obstetrical anesthesia at Cedars of Lebanon Hospital, 10-year study, 824
- premedication and anesthesia, current practices at Boston Lying-In Hospital, 341
- rooming-in program of baby with mother, observations in ward and private service, 343

HYALURONIDASE

- clinical evaluation in infertility, 304

HYDATIDIFORM MOLE

- chorionepithelioma and, 192
- Fallopian tube, 286

HYDRAMNIOS

- acute, 197

HYDRONEPHROSIS

- large, in pregnancy, 205

FETUS

- antepartum diagnosis of congenital heart disease, 649
- diabetic fertility, maternal mortality and fetal loss rate, 493
- heart tones, characteristic changes, 473
- hydrops of placenta and, with lutein cysts, 373
- intrauterine development in prolonged pregnancy, 500
- mortality and morbidity in cesarean section, 391
- reproductive system, response to administration of diethylstilbestrol and testosterone propionate in early pregnancy, 87
- roentgencephalometry, simplified method, 478
- sex, blood gonadotropins in pregnancy in relation to, 27
- tobacco, effect on estrus, pregnancy, fetal growth and lactation, 330
- water supply as determined with deuterium oxide; permeability of human placenta to water, 175

FIBRO-ADENOSIS

- effect of endocrines, 683

FIBROMYOMA (*See also under UTERUS, tumors.*)

- Fallopian tube, 285

FISTULA

- uterovesical, following therapeutic abortion, new operation, 428
- vesicovaginal, 102
- vesicovaginal, following radium treatment for cervical carcinoma, treatment, 295

FLUOROSCOPE

- advantages of hysterosalpingography under, 443

GONADOTROPHINS

- blood, in pregnancy, relation to fetal sex, 27
- chorionic, absorption and excretion when administered intramuscularly to women; comparison of aqueous, oil emulsion and wax preparations, 244
- chorionic, antihormone formation during therapy, 831
- chorionic, renal clearance in pregnancy and neoplasm of testis, 29
- placental, function, and origin of placental trophoblast, 828

- therapy, complicated by antihormone formation, 86

GONORRHEA

- in pregnancy, relation to ophthalmia neonatorum, 66

GRAFENBERG'S RING

- complications following intrauterine insertion, 455

GRANULOMA INGUINALE

- aureomycin treatment of lymphogranuloma venereum and, 633
- cervix, diagnosed clinically as carcinoma, 554
- chloromycetin, 851
- streptomycin, 410, 852
- streptomycin in ambulatory treatment, 851

GYNATRESIA

- report of 3 uncommon clinical types, 423

GYNECOLOGY

- advances in obstetrics and, 596
- basal body temperature, diagnostic use in, 1
- cancer aspect, 116
- clinical, practical application of vaginal smear, 250
- clinical, use of "phase-contrast" microscope, 311
- early ambulation in obstetrics and, 483
- gynecic symptom complexes, 730
- present position of neurosurgery in, 309
- psychiatry, report on experimental clinic, 452
- psychosomatic approach, 599
- surgery in elderly, risks and results, 143, 144
- use and misuse of hormones, 241
- venous thrombosis in obstetrics and, 394

GYNECOMASTIA

- feminizing adrenal tumor in 5-year-old boy causing, 88

HARTMAN-LITTRELL ASSAY

- etiology of fibromyomata of uterus, 107

HAWAII

- maternal mortality, 819

HEART

- block, and pregnancy, 201
- block, congenital complete, in pregnancy, 372
- cardiac indication for therapeutic abortion, 672
- cardiac patient, prognosis in pregnancy, 202

- renal clearance of chorionic gonadotrophin in pregnancy and neoplasm of testis, 29
- solitary pelvic, with vaginal aplasia, 574

LABOR

anesthesia: See ANESTHESIA.

- childbirth, design for future, 393
- following early spontaneous or artificial rupture of membranes, 783
- measurement of rate of venous blood-flow in legs of women at term and in puerperium, using radioactive sodium, 476
- pain, statistical analysis of replies to questionnaires, 479
- use of pituitrin before delivery, 459
- complications:*
 - aftercoming head, 665
 - amniotic fluid embolism, 62, 503
 - assimilation pelvis as obstetrical problem, 647
 - avulsion of completely inverted puerperal uterus as complication of manual removal of placenta, 379
 - complete bladder exstrophy, 64
 - cord complications, 382
 - delayed, 380
 - desultory, and sedation, 209
 - dystocia after amputation of cervix, 506
 - following vaginal operations, 63
 - hemorrhage attending delivery, comparison of intravenous oxytocin and ergonovine in control of, 349
 - locked twins, 505
 - obstructed, due to Naegele's pelvis, 508
 - pelvic ectopic kidney anomalies, review of literature, 737
 - penicillin therapy, effect on bacterial flora of postpartum uterus, 806
 - prolonged, management of problems, 646
 - retained placenta and postpartum hemorrhage, 804
 - ruptured uterus and other obstetric shock, massive blood transfusions in management, 801
 - ruptured uterus, diagnosis and management, study of 64 maternal deaths, 802
 - ruptures of umbilical cord, 805
 - thoracoplasty, 375
- presentation:*
 - face, 59
 - occiput posterior, management, 387

LACTATION

- tobacco, effect on estrus, pregnancy, fetal growth and, 330

LAW

- medicolegal aspects of Rh-Hr blood types, 818

LEUCORRHEA

- rational management, 531

LEVATOR ANI MUSCLE

- embryological development, 155

LIGAMENTS

- broad ligament, peritoneal bodies and cysts, 869
- round ligaments, excision in corporeal and ovarian carcinoma, 879
- uterosacral, value in uterine displacements, 885

LIVER

- function in newborn, excretion of brom-sulfalein, 662
- hepatogenic metrorrhagia of puberty, 601
- hepato-ovarian syndrome, 600
- inactivation of estradiol by rat liver in vitro, 246
- rupture in newborn, 65

LUNGS

- embolism by amniotic fluid, 62, 503

LYMPHADENECTOMY

- radical pelvic with Wertheim pan-hysterectomy, 574
- retroperitoneal lymph node dissection in cervical cancer, 878

LYMPHOGRANULOMA, *See VULVA.*

MARRIAGE

- management of rigid hymen and perineum, 850
- stability, infertility and, 152

MASTITIS

- chronic cystic, precancerous lesion? 10-year follow-up of 26 cases, 312
- chronic cystic, cancer of breast, premenstrual tension and menstrual anomalies, similarity of estrogenic effect in, 245

MATERNAL HEALTH

- and child health, 25 years in, 397

MATERNAL MORTALITY

- abortion as cause of death, 221
- analysis of period from 1937-1946 at Cincinnati General Hospital, 396
- diabetic fertility, fetal loss rate and, 493
- in Hawaii, 819

MEIGS' SYNDROME

- variant, 566

MEMBRANES

- extramembranous pregnancy, 632

HYDROPS

- fetus and placenta, lutein cysts with, 373

HYDROSALPINX

- torsion in pregnancy, 199
- unilateral, with torsion without involvement of ovary, 287

HYDROSTATIC BAG

- in obstetrics, 232

HYDROTHORAX

- pseudomucinous ovarian cyst with ascites and, 139

HYMEN

- rigid perineum and, management in early marriage, 850

HYPEREMESIS GRAVIDARUM

- 207

- with retinal hemorrhage, 486

HYPERLIPEMIA, See BLOOD, diseases.**HYPERPLASIA, See UTERUS.****HYPERTENSION**

- caused by vasopressor drugs in obstetrics, cerebral complications, 789
- chronic, does eclamptogenic toxemia cause?, 184
- effect of minimal sodium diet on blood pressure of ambulatory subjects, 189
- essential, mechanism of fall in arterial pressure produced by high spinal anesthesia, 227
- new tools for physiologic study in toxemia of pregnancy, 605
- pregnancy following Smithwick operation, 46

HYSTERECTOMY, See UTERUS, excision.**HYSTEROSALPINGOGRAPHY**

- 592
- advantages under fluoroscopic control, 443
- cervical obturation with inflatable cannula, 729
- tubal patency tests, 439
- water-soluble contrast medium, 305

INDIA

- obstetrical service, 223

INFARCTION

- uterus, 558

INFECTION

- extraperitoneal cesarean section in profoundly infected patient, 668
- supravaginal extraperitoneal cesarean section, choice for infected patient, 67
- urinary tract, in pregnancy, 642

INFERTILITY, See STERILITY.**INJURY**

- rectal, following radium treatment of cervical cancer, 259
- vaginal, at coitus, 256

INSUFFLATION

- blocked Fallopian tubes, pressure treatment, 439
- intratracheal, death of newborn infant, 660
- tubal, 592
- tubal patency tests, 439
- uterotubal, cervical obturation with inflatable cannula, 729

INTERSTITIAL TISSUE

- hermaphrodite, 91

INTESTINES

- changes secondary to irradiation of pelvic malignancies, 130
- destruction, and criminal abortion, 827
- ileal obstruction caused by endometriosis, 538
- obstruction and myomectomy in pregnancy, 579
- small bowel obstruction, endometriosis causing, 274
- strangulation in pouch of Douglas hernia, procidentia complicated by, 279

ISOTOPES, RADIOACTIVE

- measurement of rate of venous blood-flow in legs of women at term and in puerperium using radioactive sodium, 476
- rate of renewal in woman of water and sodium of amniotic fluid as determined by tracer techniques, 176
- tissue localization and excretion routes of radioactive dibromestron, 90

JELLY

- efficacy alone as contraceptive agent, 399

KETOSTEROIDS

- urinary excretion of estrogenic substances and 17-ketosteroids in metropathia hemorrhagica, 403
- urinary excretion of 17-ketosteroids determined by Zimmermann reaction, 404

KIDNEY

- hydronephrosis in pregnancy, 205
- pelvic ectopic kidney anomalies, complicating pregnancy and labor, review of literature, 737

NEPHRITIS

- termination of pregnancy in diabetes and, 676

NERVE BLOCK

- regional, treatment of eclampsia, 350

NEURECTOMY

- presacral, 882
- primary dysmenorrhea, 113 cases treated by, 838

NEUROSURGERY

- present position in gynecology, 309

NEWBORN

- birth, infant death and stillbirth data, Wisconsin, 1947, 222
- birthweight, relation to subsequent maternal diabetes mellitus, 50
- liver function, excretion of brom-sulfalein, 662
- maternal and child health, 25 years in, 397
- ossification centers, prevalence and distribution, 661
- rooming-in program, observations in ward and private service, 343
- sex ratio, experimental studies demonstrating controlled variations, 810

mortality:

- and morbidity, in cesarean section, 391
- birth, infant death and stillbirth data, Wisconsin, 1947, 222
- from intratracheal insufflation, 660

pathology:

- asphyxia and the vernix membrane, 808
- breathing irregularities, 812
- death from intratracheal insufflation, 660
- erythroblastosis associated with Rh-positive mothers, 67
- erythroblastosis, reproductive histories of mothers of 322 infants, 650
- erythroblastosis treated by replacement transfusion via umbilical vein, 214, 218
- hemolytic disease, criteria of severity, 653
- idiopathic epilepsy, birth primacy and, 66
- iso-sensitization, Coombs test in detection of, 217
- mongolism, role of maternal illness during pregnancy in etiology, 655
- ophthalmia neonatorum, gonorrhea in pregnancy related to, 66
- opisthotonus, 814
- pneumonia resulting from inhalation of gastric contents, 654
- rupture of liver and spleen, 65

- umbilical cord, intrapartum ruptures, 805
- prematurity:*

- new classification and nomenclature for newborns, including prematures and abortions, 212
- physiologic approaches, 814
- retrolental fibroplasia, 656
- vernix caseosa and subnormal temperature, 219

NICOTINIC ACID, *See VITAMINS.*

NITRAZINE TEST

- diagnosis of ruptured fetal membranes, 347

NUTRITION

- dietary and clinical study of gravidæ with reference to toxemia, 180
- low sodium diet and rice diet, effect on arterial blood pressure, 638
- minimal sodium diet, effect on blood pressure of ambulatory hypertensives, 189
- special diets, role in treatment of female infecundity, 588

OBSTETRICS

- advances in gynecology and, 596
 - basal body temperature, diagnostic use in, 1
 - childbirth, design for future, 393
 - early ambulation in gynecology and, 483
 - hydrostatic bag, 232
 - service in India, 223
 - use and misuse of hormones, 241
 - venous thrombosis in gynecology and, 394
- OCIPUT POSTERIOR POSITION, *See LABOR, presentation.*

OKLAHOMA CITY

- Wertheim hysterectomy experience, 573

OLIGURIA

- and anuria in pregnancy toxemia, 634

OPHTHALMIA NEONATORUM

- gonorrhea in pregnancy, relation to, 66

OPISTHOTONUS

- fetalis, 814

OSTEITIS

- pubis, following ureterolithotomy, 722

OVARY

- agenesis, case report with postmortem findings, 716
- aging processes in ovaries of mice belonging to strains differing in incidence of mammary carcinoma, 711
- anomalies, 159

- isthmic mucous membrane of uterus, 695
- parturition following early rupture, both spontaneous and artificial, 783
- ruptured, diagnosis by simplified vaginal smear technique, 346
- MENOMETRORRHAGIA, *See* MENSTRUATION, disorders, and UTERUS.
- MENOPAUSE
 - dangers in management, 524
 - estradiol pellet implantation in treatment, 844
 - estrogens, indiscriminate use, 404
 - meprane in treatment, 97
 - physiology, 689
 - postmenopausal cystic glandular hyperplasia of endometrium, 542
 - postmenopausal women, vaginal cytology, 529
- MENSTRUATION
 - coagulability of menstrual fluid, 408
 - hormonal factors involved in regulation of basal temperature in menstrual cycle and pregnancy, 100
 - newer concepts, 526
 - tobacco, effect on estrus, pregnancy, fetal growth and lactation, review of literature, 330
- disorders:
 - amenorrhea, induction of bleeding with precipitate estrone and progesterone, 95
 - amenorrhea, secondary, treated with low dosage irradiation of ovaries and pituitary gland, 842
 - amenorrheas, progesterone privation test or medical curettage, application in diagnosis and classification, 519
 - amenorrheas treated with progesterone and parasympatheticomimetic substances, histological studies, 407
 - dysmenorrhea, essential, pathogenesis and treatment, 687
 - dysmenorrhea, essential, role of uterine motility, 94
 - dysmenorrhea, intractable, surgical treatment, 883
 - dysmenorrhea, primary, 113 cases treated by neurectomy, 838
 - functional disorders, proper management, 523
 - hormone control of cycle, application of physiologic concepts to therapy, 837
 - metropathia, urinary excretion of estrogenic substances and 17-ketosteroids in, 403
 - metrorrhagia, hepatogenic, of puberty, 601
 - metrorrhagia of puberty due to late congenital syphilis, 527
 - metrorrhagias coexisting with ovarian tumors, mechanism, 567
 - premenstrual tension, menstrual anomalies, chronic cystic mastitis and cancer of breast, similarity of estrogenic effect in, 245
- MESONEPHROS
 - remnants in cervix, 704
- METABOLISM
 - cerebral blood flow and, in normal and toxemic pregnancy, 363
- METAPLASIA
 - epithelial, of urinary tract, 141
- MICROSCOPE
 - "phase-contrast," use in clinical gynecology, 311
- MINNEAPOLIS
 - cesarean section, 1946, 224
- MONGOLISM
 - maternal illness in pregnancy, role in etiology, 655
 - prenatal maternal factors, 816
- MUCOSA
 - vaginal, atrophy, 848
- MUCUS
 - cervical, cyclic variations and their clinical significance, 614
 - cervical, observations on crystallization, 536
 - cervical, penetration by spermatozoa, 589
 - Sims test and male infertility, 590
- MUSCLE
 - levator ani, embryological development, 155
 - perineal, progressive resistance exercise in functional restoration, 154
 - rectus abdominis, hematoma simulating gynecological disease, 888
- MYOMECTOMY
 - 577
 - intestinal obstruction and, in pregnancy, 579
- MYXEDEMA
 - uterotubal persufflation curve, effect of thyroid therapy, 682
- NAEGELE, *See* PELVIS.
- NEGRO
 - sickle cell trait, incidence and influence in gravidæ, 377

- hormonal, indications in therapy of endocrine and gynecic disorders, 520
- PELVIMETRY** (*See also PELVIS.*)
 - measurement of anterior obstetrical sagittal diameter, 787
 - radiographic technics, evaluation, 337
- PELVIS**
 - assimilation pelvis as obstetric problem, 647
 - cancer, advanced, radical surgery, 699
 - cancer, observations on delay period in diagnosis, 547
 - capacity, estimation of, 335
 - carcinoma, advanced, complete excision of viscera for, 430
 - conservative surgery, value of, 451
 - contracted, investigation and treatment of "border-line" cases, 333
 - inflammatory disease, study and classification, 870
 - Naegele's obstructed labor, 503
 - periodic examination of supposedly well women, 598
 - peritonealization following hysterectomy, simple operative procedures in intraligamentary tumors, 432
- PENICILLIN**
 - administration via vagina, 254
 - streptomycin and, in febrile obstetric and gynecologic conditions, 678
 - sulfadiazine and, prophylaxis in cesarean section, 230
 - syphilis, prenatal management, 490
 - syphilis, retreatment of gravidæ following, 57
 - syphilis, use of crystalline penicillin G in pregnancy, 492
 - therapy in obstetric patient, effect on bacterial flora of postpartum uterus, 806
- PERINEUM**
 - dissection for repair, 146
 - epithelioma and lymphogranulomatosis, vulvo-perineal, 530
 - muscles, progressive resistance exercise in functional restoration, 154
 - rigid hymen and, management in early marriage, 850
- PERIODIC EXAMINATION**
 - value in supposedly well women, 598
- PERITONEAL BODIES**
 - and cysts of broad ligament, 869
- PERITONITIS**
 - term pregnancy complicated by ruptured appendix and, 502
- PERSUFFLATION**, *See FALLOPIAN TUBES.*
- PESSARY**
 - ring, use, 313
- PHYSIOLOGY**
 - hormonal control of menstrual cycle, application of physiologic concepts to therapy, 837
 - human conception, 774
 - menopause, 689
 - new tools for study of hypertension in pregnancy toxemia, 605
 - perspectives in prematurity, 814
- PITRESSIN**, *See OXYTOCICS.*
- PITUITARY GLAND**
 - low-dosage irradiation of ovaries and, in treatment of secondary amenorrhea, 842
- PITUITRIN**, *See OXYTOCICS.*
- PLACENTA**
 - Credé's expression, 210
 - hydrops of fetus and, with lutein cysts, 373
 - manual removal, avulsion of completely inverted uterus as complication of, 379
 - nephrotoxic rabbit anti-rat placenta serum and desoxycorticosterone acetate injected in pregnant rat, 488
 - permeability to water and supply of water to human fetus as determined with deuterium oxide, 175
 - retained, and postpartum hemorrhage, 804
 - thromboplastin, soybean trypsin inhibitor preventing toxic effects of, 487
 - trophoblast origin, and function of placental gonadotrophin, 828
- accreta:*
 - previa accreta, 196
 - removed after 1½ years' retention, 385
 - with spontaneous uterine rupture in late pregnancy, 644
- previa:*
 - conservative treatment, 366
 - previa accreta, 196
 - x-ray visualization of placenta, soft-tissue cystographic techniques in diagnosis, 792
- POLIOMYELITIS**
 - acute anterior, in pregnancy, 371
 - bulbar, postmortem cesarean section after death from, 664
- POTASSIUM PERMANGANATE**
 - douche in attempted abortion, death following, 826

- bilateral herniae of uterus, tubes and, with complete congenital absence of vagina, 410
- hepato-ovarian syndrome, 600
- interstitial tissue of hermaphrodite, 91
- low dosage irradiation of pituitary gland and, in treatment of secondary amenorrhea, 842
- radiation, effects on germ plasm, 448
- sterility as related to benign lesions of uterus and, 150
- tertiary syphilis of uterus and adnexa, 597
- vascular patterns, 710
- cysts:*
 - bilateral dermoid complicating pregnancy, 54
 - large, 425
 - lutein cysts with hydrops of fetus and placenta, 373
 - preservation of function in cystic and sclerotic ovaries, 36
 - pseudomucinous, with ascites and hydrothorax, 139
 - significance of cystic enlargement with respect to treatment, 564
- function:*
 - adrenal cortical functions in grafted mouse ovaries, 93
 - control of activity, 248
 - dysfunctions and sterility, operative procedures, 883
 - insufficiency, mechanism of action of estrogenic hormone preparations in, 518
 - intermenstrual pain and time of ovulation, 840
 - ovulation, prediction of day by rat test, 96
 - ovulation, relation of intermenstrual signs and symptoms as determined by basal temperatures, 98
 - ovulation timed by rat test, insemination in treatment of sterility, 450
 - ovulation timing by basal body temperature curves, 446
 - stimulation of function through intravaginal implantation of estrogen pellets, 832
- ovarian pregnancy: See ECTOPIC PREGNANCY.*
- tumors:*
 - adenofibroma with partial differentiation to endometriosis, 718
 - and uterine bleeding, 715
 - and uterine tumors, 270
 - arrhenoblastoma, 866
 - bilateral fibroma, 565
 - carcinoma, excision of round ligaments, 879
 - dysgerminoma and fertility, 426
 - dysgerminoma, 2 cases, 427
 - estrogen-producing sertoli cell tumors (androblastoma tubulare lipoides) of testis and, 864
 - infancy and childhood, 867
 - metrorrhagias coexisting with, mechanism, 567
 - papillary cystadenocarcinoma treated with large doses of testosterone propionate, 717
 - primary teratomatous chorionepithelioma, 288
 - pseudomucinous cystadenocarcinoma, 292
 - solid teratoma, 137
 - theca cell tumors, report of 15 cases and review of literature, 291
 - variant of Meigs' syndrome, 566
 - virilizing, report of case associated with pregnancy, 289
- OVULATION, See OVARY, function.*
- OXYTOCICS*
 - abnormal uterine bleeding, arrest with pitressin, 92
 - control of hemorrhage attending delivery, comparison of intravenous oxytocin and ergonovine, 349
 - use of pituitrin before delivery, 459
- PAIN*
 - childbirth, statistical analysis of replies to questionnaires, 479
 - intermenstrual (mittelschmerz) and time of ovulation, 840
- PALMAR ERYTHEMA, See BLOOD VESSELS.*
- PAPANICOLAOU TEST, See VAGINAL SMEAR.*
- PARAMETRITIS*
 - chronic, clinical significance, 135
- PARASYMPATHETICOMIMETIC SUBSTANCES*
 - histological studies in amenorrheas treated with progesterone and, 407
- PELLETS*
 - estradiol implantation in treatment of menopause, 844
 - estrogen, intravaginal implantation, stimulation of ovarian function and induction of pregnancy, 832

- placenta previa accreta, 196
 - placenta previa, conservative treatment, 366
 - placenta previa, x-ray visualization, soft-tissue cystographic techniques in diagnosis, 792
 - poliomyelitis, acute anterior, 371
 - prediabetic, 374
 - primary torsion of normal Fallopian tube, 497
 - prolonged, 378
 - prolonged, intrauterine fetal development, 500
 - pulmonary embolism by amniotic fluid, report of fatal case and review of literature, 503
 - purpura hemorrhagica, 376
 - role of maternal illness in etiology of mongolism, 635
 - rubella, lens changes of embryo after, 659
 - septate uterus, double vagina and other congenital abnormalities, 200
 - sickle cell anemia, 798
 - sickle cell trait, incidence and influence in colored gravidae, 377
 - Smithwick operation, pregnancy following, 46
 - syphilis, penicillin therapy, 490
 - syphilis, retreatment following penicillin, 57
 - syphilis, use of crystalline penicillin G, 492
 - thoracoplasty, with special reference to childbirth, 375
 - torsion of hydrosalpinx, 199
 - trauma and interruption, 368
 - tuberculosis, 47, 369, 796
 - urinary tract infections, 642
 - uterine prolapse in second trimester, 631
 - virilizing tumors of ovary, 289
- toxemias:**
- blood pressure maintenance, evaluation of neurogenic and humoral factors using tetra-ethyl-ammonium chloride, 362
 - cerebral blood flow and metabolism, 363
 - dietary and clinical study of gravidae with reference to, 180
 - does eclamptogenic toxemia cause chronic hypertension?, 184
 - eclampsia, electroencephalographic records in relation to blood pressure changes, 40
 - eclampsia, etiology, evaluation of recent theories, 359
 - eclampsia, follow-up study, 44
 - eclampsia, physiopathology, 188
 - eclampsia, regional nerve block in treatment, 350
 - hypertension of, new tools for physiologic study, 605
 - nephrotoxic rabbit anti-rat placenta serum and desoxycorticosterone acetate injected in pregnant rat, 488
 - ocular manifestations, 637
 - oliguria and anuria, 634
 - preeclampsia, severe, treatment, 36
 - preeclamptic, anemia simulating, 489
 - sodium excretion, effectiveness of various diuretic agents, 42
 - veratrum viride, 365
 - veratrum viride, effect on urine volume, blood pressure and pulse rate, 793
- PRENANEDIOL**
- effect of diethylstilbestrol on urinary excretion in pregnancy, 781
- PREMATURITY, See NEWBORN, prematurity.**
- PRISCOL**
- physiologic study of hypertension in pregnancy toxemia, 609
- PROGESTERONE**
- amenorrheas treated with parasympatheticomimetic substances and, histological studies, 407
 - functional uterine bleeding, therapy, 679
 - induction of bleeding in amenorrhea with precipitate estrone and, 95
 - privation test, applicability in diagnosis and classification of amenorrheas, 519
 - vascular architecture of rat uterus as influenced by estrogen and, 401
- PROLACTIN**
- hyperestrogenism treated with, 243
- PROLAPSE, See UTERUS, prolapse.**
- PRURITUS**
- vaginal and rectal, etiology and treatment, 101
- PSYCHIATRY**
- gynecological, report on experimental clinic, 452
 - indications for terminating pregnancy, 675
 - psychosomatic approach to gynecologic problems, 599
- PUBERTY**
- adolescent girl, 733
 - hepatogenic metrorrhagia, 601

PREGNANCY

- basal temperature, hormonal factors involved in regulation, 100
- blood gonadotrophins during, relation to fetal sex, 27
- blood pressure maintenance, evaluation of neurogenic and humoral factors using tetra-ethyl-ammonium chloride, 362
- cerebral blood flow and metabolism, 363
- chorionic gonadotrophin, renal clearance, 29
- cigarette smoking, 331
- dietary and clinical study with reference to toxemia, 180
- diethylstilbestrol and testosterone propionate in early pregnancy, response of fetal reproductive system, 87
- diethylstilbestrol, effect on urinary excretion of pregnanediol and endogenous estrogens, 781
- diuretic effects of estrogens in last 4 months, 185
- erythrocyte sedimentation velocity, 178
- induction of pregnancy through intravaginal implantation of estrogen pellets, 832
- male toad test, 328
- maternal factors in mongolism, 816
- nicotinic acid utilization, 780
- plasma volume and extravascular fluid volume in puerperium and, 471
- rate of renewal in woman of water and sodium of amniotic fluid as determined by tracer techniques, 176
- sodium excretion, effectiveness of various diuretic agents, 42
- tobacco, effect on estrus, fetal growth, lactation and, 330
- urinary volume, effect of sedatives, 187
- vascular changes of skin, vascular spiders and palmar erythema, 777
- ectopic:*
 - 625
 - abdominal, 628
 - abdominal, following rupture of cesarean scar, 499
 - bilateral tubal, 53
 - interstitial, 4 cases following homolateral salpingectomy, 301
 - ovarian, 712, 713, 791
 - primary abdominal, in lesser peritoneal cavity, 51
 - unruptured primary ovarian, 293
 - variant of Hofstatter-Cullen sign in intra-abdominal hemorrhage from, 790
- pathology:*
 - abortion, following acute abdomen caused by corpus luteum rupture during coitus, 58
 - Addison's disease, 800
 - angina of effort, 195
 - appendicitis, acute and chronic, comparative study, 797
 - appendix, ruptured, with generalized peritonitis at term, 502
 - bilateral ovarian dermoid cysts, 54
 - cardiac patient, prognosis, 201
 - cerebral complications resulting from hypertension caused by vasopressor drugs, 789
 - choreiform behavior, 56
 - colitis, chronic ulcerative, 53
 - cord complications, 382
 - decidual bleeding, 204
 - diabetes mellitus, 495
 - diabetes mellitus, relation between infant birthweight and subsequent development of, 50
 - diabetic fertility, maternal mortality and fetal loss rate, 493
 - diabetic animals, investigation, 205
 - dicumarol treatment, dangers, 641
 - diethylstilbestrol in prevention and treatment of complications, 190
 - extramembranous, 632
 - gonorrhea, relation to ophthalmia neonatorum, 66
 - heart block, 201
 - heart block, congenital complete, 372
 - heart disease, indications for therapeutic abortion or avoidance of conception, 794
 - hydramnios, acute, 197
 - hydronephrosis, 205
 - hyperemesis, 207
 - hyperemesis, with retinal hemorrhage, 486
 - hyperlipemia, severe, in nondiabetic pregnancy, 643
 - intestinal obstruction and myomectomy, 579
 - ocular manifestations, 637
 - pelvic ectopic kidney anomalies, review of literature, 737
 - placenta accreta, removed after 1½ years' retention, 385
 - placenta accreta, with spontaneous uterine rupture in late pregnancy, 644

- effect on urinary volume of gravidæ, 187
- SEX**
 - differentiation and abnormality, role of sex hormones, 85
 - fetal, blood gonadotrophins in pregnancy in relation to, 27
 - ratio, experimental studies demonstrating controlled variations, 810
- SHOCK**
 - during continuous caudal anesthesia, 30
 - obstetric, role of massive blood transfusions in management, 801
- SICKLE CELLS**, *See BLOOD, diseases.*
- SIMS TEST**
 - male infertility, 590
- SKIN**
 - vascular changes in pregnancy, vascular spiders and palmar erythema, 777
- SMITHWICK OPERATION**
 - for hypertension, pregnancy following, 46
- SODIUM**
 - excretion in gravidæ, effectiveness of various diuretic agents, 42
 - minimal diet, effect on blood pressure of ambulatory hypertensives, 189
 - radioactive, measurement of rate of venous blood-flow in legs of women at term and in puerperium, 476
 - rate of renewal in woman of water and sodium of amniotic fluid as determined by tracer techniques, 176
- SOYBEAN TRYPSIN**
 - value in preventing toxic effects of human placental thromboplastin, 487
- SPERMATOZOA**
 - number required for fertilization, 441
 - pathology, terminology of, 449
 - penetration of cervical mucus, 589
 - Sims test and male infertility, 590
- SPINAL ANESTHESIA**, *See ANESTHESIA.*
- SPLEEN**
 - rupture in newborn, 65
- STERILITY**
 - artificial insemination, position in treatment, 441
 - as related to benign lesions of uterus and ovary, 150
 - biologic aspect in treatment, 587
 - endocrine factors in female, diagnosis and treatment, 447
 - evaluation of factors, 307
 - female, 147, 149
 - female, facts and fantasy, 303
 - fertility and dysgerminoma ovarii, 426
 - hyaluronidase, clinical evaluation, 304
 - insemination timed by rat ovulation test, 450
 - male, evaluation, 440
 - male, Sims test, 590
 - newer approaches to fertility studies, 586
 - newer aspects, 438
 - operative procedures for ovarian dysfunctions and, 883
 - problem, 306
 - recent advances in treatment, 584
 - role of special diets in treatment of female, 588
 - stability of marriage, 152
 - surgery in treatment, 443
 - tubal insemination in treatment of certain types, 591
 - use of vaginal smears in study, 445
 - why sterility?, 437
- STOMACH**
 - inhalation of contents resulting in pneumonia in newborn, 654
- STRANG CANCER PREVENTION CLINICS**, 113
- STREPTOMYCIN**
 - granuloma inguinale, ambulatory treatment with, 851
 - granuloma inguinale treated with, 852
 - penicillin and, in febrile obstetric and gynecologic conditions, 678
 - tuberculosis of endometrium treated with, 855
- SULFADIAZINE**
 - and penicillin prophylaxis in cesarean section, 230
- SUPPOSITORY**
 - efficacy as contraceptive agent, 399
- SURGERY** (*See also specific operations.*)
 - amnion, use in construction of artificial vagina, 433
 - anatomy of cystocele and urethrocele with reference to pubocervical fascia, 875
 - complete excision of pelvic viscera for advanced carcinoma: one-stage abdominoperineal operation with end colostomy and bilateral ureteral implantation into colon above colostomy, 430
 - conservative, in endometriosis, results in 138 cases, 706
 - conservative, of pelvic organs, 451
 - criminal instrumental abortions, dangers, 398

- metrorrhagia due to late congenital syphilis, 527
- precocious, in girls, 835
- precocious, in 3-year-old girl, 562
- PUBIS
 - osteitis, following ureterolithotomy, 722
- PUERPERIUM
 - hemorrhage, and retained placenta, 804
 - hemorrhage, primary postpartum, 383
 - measurement of rate of venous-flow in legs of women at term and in puerperium, using radioactive sodium, 476
 - plasma volume and extravascular fluid volume in pregnancy and, 471
 - uterine bacterial flora, effect of penicillin therapy, 806
- PULSE RATE
 - effect of veratrum viride in normal and toxemic pregnancy, 793
- PURPURA
 - hemorrhagica, in pregnancy, 376
- PYOMETRA
 - ruptured, as surgical emergency, 853
- PYOSALPINX, *See FALLOPIAN TUBES.*
- PYRIDOXINE
 - effect on blood urea, 639
- RADIATION THERAPY
 - Bartholin's glands carcinoma, radium, 881
 - cervical cancer, 5-year end-results of irradiation therapy at Memorial Hospital, 420
 - cervical cancer, rectal injuries following radium treatment, 259
 - cervical carcinoma, repair of vesicovaginal fistula following radium treatment, 295
 - corpus carcinoma, 264
 - corpus carcinoma and fibroid, treated with radium and hysterectomy, 268
 - endometrial carcinoma, adjunctive radiation in surgical treatment, 131
 - germ plasm, effects of radiation, 448
 - intestinal changes secondary to irradiation of pelvic malignancies, 130
 - intracavitary radiation in adenocarcinoma, uterus, histological findings following, 723
 - low dosage irradiation of ovaries and pituitary gland in treatment of secondary amenorrhea, 842
 - radium in conjunction with gynecologic surgery, 723
 - recurrent and uncontrolled cancer after irradiation and conservative surgery, surgical problem, 877
 - urethral carcinoma, radium, 720
 - vaginal carcinoma in 14-year-old girl treated by, 532
 - vaginal radium, simple method of applying, 887
- RADIOGRAPHY
 - fetal roentgencephalometry, simplified method, 478
 - pelvimetric technics, evaluation, 337
 - roentgenography of vaginal cysts, 845
 - x-ray visualization of placenta, soft-tissue and cystographic techniques in diagnosis of placenta previa, 792
- RADIUM, *See RADIATION THERAPY.*
- RAT TEST
 - insemination timed by, treatment of sterility, 450
 - ovulation, prediction of day as confirmed by 50 conceptions, 96
- RECTUM
 - injuries following radium treatment of cervical cancer, 259
 - pruritus, etiology and treatment, 101
- REPRODUCTIVE SYSTEM
 - fetal, response to administration of diethylstilbestrol and testosterone propionate in early pregnancy, 87
 - vascular congestion and hyperemia, effect on structure and function of, 593
- RESPIRATION
 - irregularities in newborn period, 812
- RETINA
 - hemorrhage, hyperemesis gravidarum with, 486
- RETROLENTAL FIBROPLASIA
 - premature infants, 656
- RH FACTOR, *See BLOOD, groups.*
- ROMAN CATHOLIC
 - views on termination of pregnancy, 673
- ROOMING-IN PROGRAM
 - observations in ward and private service, 343
- RUBELLA
 - lens changes of embryo after, 659
- SALPINGECTOMY
 - homolateral, 4 cases of interstitial pregnancy following, 301
- SCOPOLAMINE, *See ANESTHESIA.*
- SEDATIVES
 - desultory labor and, 209

TOXEMIA, *See* PREGNANCY, *toxemias*.

TRANSFUSION, *See* BLOOD.

TRAUMA

— interruption of pregnancy, 368

TRICHOMONAS VAGINALIS, *See* VAGINA.

TROPHOBLAST

— placental, origin, and function of placental gonadotrophin, 828

TUBERCULOSIS

— adenomyosis of uterus with tuberculous infection, 282

— cervix, case which macroscopically resembled cervical carcinoma, 267

— childbearing in, 47

— endometrium, treated with streptomycin, 855

— pregnancy, 369, 796

— therapeutic abortion, 674

— thoracoplasty and pregnancy, with special reference to childbirth, 375

TUMORS (*See also under regions and organs.*)

— adrenal cortex, in mice, sex hormone secretion by, 681

— feminizing adrenal, causing gynecomastia in 5-year-old boy, virilizing tumor in 5-year-old girl, 88

— heterologous, of cervix, 557

— homologous ovarian and testicular, 864

— intraligamentary, simple operative procedures with notes on peritonealization of pelvis following hysterectomy, 432

— ovarian, in infancy and childhood, 867

— syncytioma, syncytial endometriosis, 110

— testis, renal clearance of chorionic gonadotrophin in pregnancy and, 29

— uterine and ovarian, a consideration, 270

— virilizing, of ovary, case associated with pregnancy, 289

TWINS

— locked, 505

— pseudohermaphroditism, 731

ULCERS

— acute non-venereal genital, 411

UMBILICAL CORD

— complications during pregnancy and labor, 382

— replacement transfusion for erythroblastosis via umbilical vein, 214, 218

— ruptures, case of intrapartum rupture of all 3 vessels, 805

UREA

— blood, effect of pyridoxine, 639

URETEROLITHOTOMY

— osteitis pubis following, 722

URETHRA

— carcinoma, radium therapy, 720

— caruncle, relationship to carcinoma of urethra, 140

— diverticulum, 570

— urethrocele, surgical anatomy, with reference to pubocervical fascia, 875

URETHROCELE, *See* URETHRA.

URINARY TRACT

— changes in cervical carcinoma, 873

— epithelial metaplasia, 141

— infections during pregnancy, 642

URINE

— excretion of estrogenic substances and 17-ketosteroids in metropathia hemorrhagica, 403

— excretion of pregnanediol and endogenous estrogens in pregnancy, effect of diethylstilbestrol, 781

— excretion of 17-ketosteroids determined by Zimmermann reaction, 404

— volume, effect of veratrum viride in normal and toxemic pregnancy, 793

— volume in gravidæ, effect of sedatives, 187

UTERUS

— adenomyosis of corpus, fibroadenoma of cervix, 854

— adenomyosis with tuberculous infection, 282

— bicornate, ruptured horn, 556

— bilateral herniae of tubes, ovaries and, with complete congenital absence of vagina, 410

— endometrial growth in monkeys, 107

— endometritis and metritis, acute decidual, 543

— endometrium, atypical hyperplasia simulating adenocarcinoma, 127

— endometrium, effects of prolonged diethylstilbestrol therapy, 686

— endometrium, histochemical studies on abnormal growth, 424

— endometrium, histology in functional hemorrhage, 535

— endometrium, postmenopausal cystic glandular hyperplasia, 542

— endometrium, tuberculosis treated with streptomycin, 855

- endometriosis, treatment, 861
- excision of cysts of Bartholin's gland, 880
- excision of round ligaments in corporeal and ovarian carcinoma, 879
- gynecologic, efficacy of certain drugs in promoting bladder evacuation after, 721
- gynecologic, in elderly, risks and results, 143, 144
- gynecologic, radium in conjunction with, 723
- intractable dysmenorrhea, treatment, 883
- neurosurgery, present position in gynecology, 309
- perineal dissection for repair, 146
- presacral neurectomy, 882
- preservation of function in cystic and sclerotic ovaries, 136
- radical, for advanced pelvic cancer, 699
- radical operation for cancer of cervix, 418
- reconstructive, of vagina, histologic study of structural components, 691
- recurrent and uncontrolled cancer after previous irradiation and conservative surgery, surgical problems, 877
- retroperitoneal lymph node dissection in cervical cancer, 878
- role in treatment of cervical carcinoma, 575
- simple operative procedures in intra-ligamentary tumors with notes on peritonealization of the pelvis following hysterectomy, 432
- sterility and ovarian dysfunctions, procedures for, 883
- treatment of endometrial carcinoma, evaluation of adjunctive radiotherapy, 131
- treatment of genital prolapse, 583
- treatment of sterility, 443
- treatment of uterine myomata, 577
- treatment of uterine retrodeviation and prolapse, 582
- uterosacral ligaments, value in uterine displacements, 885
- uterovesical fistula following therapeutic abortion, new operation, 428
- vaginal, outcome of pregnancy following, 63

SUSPENSION

- retroflexed uterus, 695

SYMPTOMS

- gynecic complexes, 730

SYPHILIS

- crystalline penicillin G in pregnancy, 492

- late congenital, metrorrhagia of puberty due to, 527
- prenatal management, penicillin therapy, 490
- retreatment of gravidæ following penicillin, 57
- tertiary, of uterine body and adnexa, 597

TEMPERATURE

- basal body, determining relation of intermenstrual signs and symptoms to ovulation, 98
- basal body, diagnostic use in gynecology and obstetrics, 1
- basal body, hormonal factors involved in regulation of, in menstrual cycle and pregnancy, 100
- basal body, ovulation timing by, 446
- basal, cause of physiologic changes, 99
- subnormal, in prematures, and vernix caseosa, 219

TESTIS

- estrogen-producing sertoli cell tumors (androblastoma tubulare lipoides) of ovary and, 864
- neoplasm, renal clearance of chorionic gonadotrophin in pregnancy and, 29

TESTOSTERONE

- administered in early pregnancy, response of fetal reproductive system, 87
- advanced breast carcinoma, treatment, 830
- papillary cystadenocarcinoma of ovary treated with large doses, 717

TETRAETHYLAMMONIUM CHLORIDE

- evaluation of neurogenic and humoral factors in blood pressure maintenance in normal and toxemic pregnancy, 362

THORACOPLASTY

- pregnancy, with special reference to childbirth, 375

THROMBOPLASTIN, *See* BLOOD.

THROMBOSIS

- venous, in obstetrics and gynecology, 394

THYROID

- uterotubal persufflation curve in myxedema, effect of therapy, 682

TOAD TEST

- male, for pregnancy, 328

TOBACCO

- cigarette smoking in pregnancy, 331
- effect on estrus, pregnancy, fetal growth and lactation, review of literature, 330

excision:

- abdominal total hysterectomy with modifications in technique, 725
- carcinoma of corpus and fibroid treated with radium and hysterectomy, 268
- cesarean hysterectomy at Chicago Lying-In Hospital, 69
- complete excision of pelvic viscera for advanced carcinoma, 430
- frequency of hysterectomy for benign disease, 300
- radical surgery for advanced pelvic cancer, 699
- simple operative procedures in intraligamentary tumors with notes on peritonealization of pelvis following hysterectomy, 432
- statistical report of 1771 hysterectomies, 572
- subtotal hysterectomy, fibroid in cervical stump after, 299
- total versus subtotal hysterectomy, 576
- total vs. subtotal hysterectomy with reference to cervical carcinoma, 435
- vaginal hysterectomy, 573
- vaginal hysterectomy, 800 cases, 298
- vaginal hysterectomy followed by vaginal endometriosis, 533
- vaginal hysterectomy for cancer of uterus and vagina, 296
- Wertheim hysterectomy, experience in Oklahoma City, 573
- Wertheim operation in retrospect, 726
- Wertheim panhysterectomy and radical lymphadenectomy, 574

hemorrhage:

- 112
- abnormal, 559
- abnormal, arrest with pitressin tannate in oil, 92
- and ovarian tumors, 715
- functional, progesterone therapy, 679
- induction of bleeding in amenorrhea with precipitate estrone and progesterone, 95

inversion:

- avulsion of inverted uterus as complication of manual removal of placenta, 379
- new concepts in replacement, 667

malposition:

- displacements, value of uterosacral ligaments, 885
- retrodeviation and prolapse, surgical treatment, 582
- retroflexion and suspension, 695

prolapse:

- carcinoma of cervix complicating, 126
- colpectomy in management, 886
- complicated by intestinal strangulation in pouch of Douglas hernia, 279
- in second trimester of pregnancy, 631
- surgical treatment, 583
- surgical treatment of retrodeviation and, 582

rupture:

- diagnosis and management, study of 64 maternal deaths, 802
- massive blood transfusions in management, 801
- ruptured pyometra as surgical emergency, 853
- spontaneous, in late pregnancy with placenta accreta, 644

tumors:

- and ovarian tumors, a consideration, 270
- chorionepithelioma, mixed mesodermal tumor and leiomyosarcoma, clinical pathological conference, 277
- fibroid, and corpus carcinoma, treated with radium and hysterectomy, 268
- fibroid in cervical stump after subtotal hysterectomy, 299
- fibromyomata, etiology, 107
- intestinal obstruction and myomectomy in pregnancy, 579
- leiomyomas, development in rats with endocrine imbalance, 684
- leiomyosarcoma, report of 16 cases, 1917-1948, 703
- "mesodermal mixed" tumor, 269
- myomata, surgical treatment, 577
- myomectomy, 577
- sarcoma, 134, 857
- sarcoma, inoperable, 10-year survival of patient, 422
- sarcoma, report of 2 cases with generalized metastasis, 132
- sarcomatous degeneration of myoma found at cesarean section, 421
- stromal endometriosis, 540

VAGINA

- absence, complete congenital, with bilateral herniae of uterus, tubes and ovaries, 410
- aplasia, with solitary pelvic kidney, 874
- artificial, use of amnion in construction, 433
- atresia, partial, 255

- gynatresia, 3 uncommon clinical types, 423
- histological studies in amenorrheas treated with progesterone and parasympatheticomimetic substances, 407
- hyperplasia and cancer, 550
- infarction, 558
- isthmic mucous membrane, 695
- motility, role in essential dysmenorrhea, 94
- parametritis, chronic, clinical significance, 135
- septate, and double vagina with pregnancy, 200
- sterility as related to benign lesions of ovary and, 150
- syphilis, tertiary, of adnexa and, 597
- vascular architecture of rat uterus as influenced by estrogen and progesterone, 401
- carcinoma: (See also UTERUS, cervix.)*
- adenocarcinoma, histologic findings following intracavitary radiation, 723
- and fibroid, treated with radium and hysterectomy, 268
- and vagina, vaginal hysterectomy for, 296
- detection, early, by simple screening methods, 121
- diagnosis by vaginal and uterine secretions, 697
- diagnosis by vaginal smear, silver carbonate stain, 120
- diagnosis, cervical smear, 544, 546
- diagnosis, colpocytological method, 122
- diagnosis, early, 112
- diagnosis, early, Papanicolaou test, 416
- endometrial, adjunctive radiotherapy in surgical treatment, 131
- evolution in rabbit, 280
- excision of round ligaments, 879
- fundus, treatment, 124
- hyperplasia and, 550
- in one horn of uterus bicornu unicollis, 857
- radiation treatment, 264
- radical operation for, 418
- cervix:*
- amputation, dystocia after, 506
- cancer, diagnosis preclinical, use of cervical cone knife in patients with positive vaginal smear, 417
- cancer, 5-year end-results of irradiation therapy at Memorial Hospital, 420
- cancer, pre-invasive, 701
- cancer, rectal injuries following radium treatment, 259
- cancer, retroperitoneal lymph node dissection, 878
- cancer, treatment in local tumor clinics, 550
- cancer, unsuspected, in gynecologic patients, 700
- carcinoma, comparison of accuracy in diagnosis of vaginal smear and biopsy, 123
- carcinoma, complicating procidentia uteri, 126
- carcinoma, early, cytologic diagnosis, 414
- carcinoma, *in situ*, smear diagnosis, 118
- carcinoma, modern concepts, 315
- carcinoma, necropsy findings, implications for treatment, 702
- carcinoma of vulva and, treatment, 105
- carcinoma, repair of vesicovaginal fistula following radium treatment, 295
- carcinoma, retreatment, 549
- carcinoma, role of surgery in treatment, 575
- carcinoma, therapeutic problem, 856
- carcinoma, total vs. subtotal hysterectomy, 435
- carcinoma, treatment, 266
- carcinoma, urinary tract changes, 873
- cervical smear in diagnosis of uterine cancer, 544
- cervicitis, chronic, histological basis for treatment, 555
- chorionepithelioma, 552
- conization, wide, 580
- endometriosis, primary, 860
- fibroadenoma, with adenomyosis of corpus, 854
- fibroid in stump after subtotal hysterectomy, 299
- granuloma inguinale of cervix diagnosed clinically as carcinoma, 554
- mesonephric remnants, 704
- mucus, cyclic variations and their clinical significance, 614
- mucus, observations on crystallization, 536
- mucus, penetration by spermatozoa, 589
- obturation with inflatable cannula in tubal insufflation and hysterosalpingography, 729
- tuberculosis, case which macroscopically resembled cervical carcinoma, 267
- tumor, heterologous, 557

- epithelioma and lymphogranulomatosis, vulvo-perineal, 530
- fibromyxoma, 257
- granuloma inguinale, ambulatory treatment with streptomycin, 851
- granuloma inguinale treated with chloromycetin, 851
- granuloma inguinale treated with streptomycin, 410, 852
- lymphogranuloma venereum and granuloma inguinale treated with aureomycin, 633
- malignancy, 103
- ulcers, acute non-venereal, 411

WATER

- permeability of placenta to, and supply to fetus as determined with deuterium oxide, 175

- rate of renewal in woman of water and sodium of amniotic fluid as determined by tracer techniques, 176

WEIGHT

- infant birthweight, relation to subsequent maternal diabetes mellitus, 50

WERTHEIM OPERATION, *See* UTERUS, *excision*.

WISCONSIN

- birth, infant death and stillbirth data, 1947, 222

X-RAY, *See* RADIATION THERAPY and RADIOGRAPHY.

ZIMMERMANN REACTION

- urinary excretion of 17-ketosteroids determined by, 404

- atrophy of mucosa, 848
 - bacteriology in 75 normal young adults, 847
 - cancer of uterus and, vaginal hysterectomy, 296
 - carcinoma in 14-year-old girl treated by radiation, 532
 - cysts, roentgenography, 845
 - Döderlein's bacillus, technique for isolation, maintenance and culture, 534
 - double, and septate uterus with pregnancy, 200
 - endometriosis following vaginal hysterectomy, 533
 - estrogenic preparations, effects on mucosa, 84
 - false, formed by coitus, 845
 - implantation of estrogen pellets, 832
 - injury at coitus, 256
 - leucorrhea, rational management, 531
 - melanoma, primary, 253
 - operations, outcome of pregnancy following, 63
 - penicillin administration via, 254
 - prolapse of uterus and, colpectomy in management, 886
 - pruritus, etiology and treatment, 101
 - radium, simple method of applying, 887
 - reconstructive surgery, histologic study of structural components, 691
 - rupture of vault at coitus, 256
 - trichomonad infestations, cultural method for diagnosis, 692
 - vaginitis, amoebic, 846
 - vaginitis, senile, use of estrogenic cream, 692
 - vaginitis, *Trichomonas*, atabrine in treatment, 258
 - vesicovaginal fistula, 102
 - vesicovaginal fistula following radium treatment for cervical carcinoma, repair, 295
- VAGINAL SMEAR**
- acidophilic atrophic vaginal epithelium in postmenopausal women, 529
 - assay of estrogens given orally or intramuscularly, 247
 - cervical smear in diagnosis of uterine cancer, 544
 - cytologic diagnosis of uterine cancer by vaginal and uterine secretions, 697
 - cytologic variations in postmenopausal women, 529
 - cytology as diagnostic method in early cervical carcinoma, 414
 - diagnosis of cervical carcinoma, comparison of accuracy of biopsy and, 123
 - diagnosis of genital cancer, 113, 119, 120, 122, 415, 416, 546, 698
 - diagnosis of *in situ* cervical carcinoma, 118
 - diagnosis of preclinical cervical cancer, use of cervical cone knife in patients with positive smear, 417
 - diagnosis of ruptured fetal membranes by use of simplified smear technique, 346
 - practical application in clinical gynecology, 250
 - silver carbonate stain for diagnosis of uterine cancer, 120
 - use in study of sterility, 445
- VASCULAR SPIDERS, See BLOOD VESSELS.**
- VASOPRESSOR DRUGS**
- causing hypertension and cerebral complications in obstetrics, 789
- VEINS**
- measurement of rate of blood-flow in legs of women at term and in puerperium, using radioactive sodium, 476
 - thrombosis in obstetrics and gynecology, 394
 - umbilical, replacement transfusion for erythroblastosis via, 214, 218
- VERATRUM VIRIDE**
- effect on urine volume, blood pressure and pulse rate in normal and toxemic pregnancy, 793
 - physiologic study of hypertension in pregnancy toxemia, 609
 - toxemias of pregnancy, 365
- VERNIX CASEOSA**
- asphyxia neonatorum and, 808
 - subnormal temperature in prematures, 219
- VITAMINS**
- B deficiency, inactivation of estrogenic hormone by women with, 240
 - nicotinic acid, utilization by gravidæ, 780
- VULVA**
- Bartholin's gland, carcinoma, radium therapy, 881
 - Bartholin's gland, cysts, excision, 880
 - Bartholin's gland, primary carcinoma, 106
 - carcinoma of cervix and, treatment, 105
 - cylindroma: adenocarcinoma, cylindroma type, 693

- Causey, G. C., 292
 Chalmers, J. A., 285, 286, 376
 Chapman, J. C. F., 695
 Charleswood, G. P., 845
 Check, F., 447
 Chesley, L. C., 44, 184
 Chesner, C., 67
 Chester, R. V., 820
 Chisholm, T. C., 867
 Chisholm, W. N., 196
 Christie, A., 661
 Cirerrella, J. A., 67
 Clain, A., 853
 Clayton, B. E., 781
 Cleland, J. G. P., 821
 Cobb, S. W., 315
 Cofer, O. S., 885
 Cogswell, R., 777
 Cole, H. H., 248
 Collier, T. W., 731
 Colvin, E. D., 349
 Conrad, K. K., 479
 Cooper, C. L., 827
 Corbet, R. M., 205
 Corbett, R. M., 857
 Cordes, F. C., 659
 Cornell, E. L., 101
 Corrozzino, O. M., 57
 Cosgrove, S. A., 209
 Costolow, W. E., 116
 Coulton, D., 97
 Counsellor, V. S., 570
 Cowie, D. B., 176
 Craig, S. E., 576
 Crawford, O. B., 820
 Crisp, W. J. C., 853
 Cromer, J. K., 122
 Cross, J. B., 492
 Crossen, R. J., 106, 580
 Crowell, J. A., 874
 Culiner, A., 311
 Curtis, A. H., 270
 Cutbush, M., 653
 Cuyler, W. K., 113, 529, 698
 Danforth, D. N., 695
 Danforth, W. C., 298
 da Paz, A. C., Jr., 591
 Darling, M. A., 159
 Davids, A. M., 143
 Davidsohn, I., 215
 Davis, A., 309
 Davis, G. H., 703
 Davis, M. E., 87, 99, 147
 Dearnley, G., 590
 De Costa, E. J., 110
 de la Balze, F. A., 519
 Delascio, D., 597
 Delson, B., 710
 De Meio, R. H., 246
 de Moraes, A., 577
 de Santiago, A. P., 682
 de Soldenhoff, R., 282
 Detweiler, H. K., 674
 Deweese, W. J., 713
 Dexter, M., 777
 Diamond, L. K., 214
 Dick, F., Jr., 808
 Diddle, A. W., 98, 256, 368, 866
 Dieckmann, W. J., 69
 Diehl, W. K., 94, 873
 Dienst, R. B., 851
 Diggs, E. S., 723
 D'Ingianni, V., 274
 Dockerty, M. B., 538
 Dodds, E. C., 595
 Donato, V. M., 553, 557
 Donnelly, G. C., 105
 Donnelly, J. F., 634
 Dougal, D., 268
 Douglas, G. F., 150
 Douglas, R. G., 230
 Drell, M. J., 637
 Drewes, E. L., 274
 Dubrausky, V., 407
 Dula, F. M., 258
 Dunlop, D. M., 493
 Eastman, N. J., 399
 Eckman, P. F., 277
 Edmonds, D. G., 476
 Edwards, J. L., 269
 Ehrenberg, C. J., 224
 Ellis, H. B., 664
 Ellison, E. T., 550
 Elzey, N. D., 51
 Embick, J. F., 777
 Emge, L. A., 284
 Engelman, M., 90
 Esselborn, V. M., 837
 Evans, A. L., 885
 Evans, A. M., 266
 Evans, H. D., 486
 Fallon, J., 790
 Farell, D. M., 524
 Farris, E. J., 96, 450
 Fee, M. G., 791

AUTHOR INDEX

VOLUME 4, 1949

- Abrams, R., 533
 Acosta-Sison, H., 551
 Adriani, J., 31, 72
 Albert, A., 29
 Allen, W. M., 451
 Allgood, J. L., 478
 Alter, M. M., 543
 Anderson, G. W., 737, 798
 Andrews, M. C., 806
 Angrist, A., 660
 Aragon, G. T., 69
 Armstrong, W. C., 47
 Arneson, A. N., 117
 Arnold, W. T., 686
 Ashton, D. L., 126
 Asirvathan, J., 223
 Assali, N. S., 232, 362, 396, 605, 793
 Atkins, H. J. B., 683
 Atkinson, W. B., 100, 424
 Austin, B. R., 46
 Austin, C. R., 441
 Ayre, J. E., 417

 Bacon, W. B., 706
 Baker, J. K., 289
 Ball, T. L., 426
 Barber, A., 659
 Barcham, J., 789
 Barnes, J., 592
 Barns, H. H. F., 374, 495
 Bartholomew, R. A., 349
 Bartley, M. D., 643
 Barton, M., 588, 590
 Bauer, A. R., 812
 Bauld, W. A. G., 105
 Baxter, J., 665
 Bayle, M. A., 715
 Beacham, D. W., 439, 642
 Beacham, H. T., 642
 Beacham, W. D., 439, 642
 Bean, W. B., 777
 Beard, R., 380
 Beerman, H., 57
 Bellas, J. E., 102
 Belt, E., 692
 Benda, C. E., 816
 Bender, S., 267
 Benefield, M. L., 421
 Benson, R. C., 92

 Bernhard, P., 331
 Bernstine, J. B., 66
 Bickers, W., 544
 Bjork, F. J., 69
 Black, E. F. E., 185
 Black, M. G., 482
 Bland, G. W., 66
 Blumer, C. E. M., 269
 Bolton, J. P., 712
 Bonney, V., 726
 Boog, J. M., 819
 Booth, A., 842
 Bowing, H. H., 881
 Bowles, H. E., 805
 Bowley, C. C., 372
 Bradbury, J. T., 42, 187, 244, 247, 831
 Branch, W. E., 827
 Brooks, E. F. J., 673
 Brown, J. A., 103, 225
 Brown, J. M., 481
 Brown, R. C., 587
 Brown, W. E., 42, 187, 244, 247
 Brown, W. W., 188
 Brown, W. W., Jr., 315
 Browne, O'D., 838
 Brumfield, F. O., 801
 Brunschwig, A., 418, 420, 430, 699, 702, 877
 Brust, A. A., 362
 Bryant, R. D., 396
 Brzezinski, A., 240
 Burdman, M., 256
 Burger, K., 373, 407, 432, 433
 Burns, E. L., 416
 Burnside, A. F., 275
 Burr, H. S., 546
 Burton-Brown, J. R. C., 200
 Busby, T., 798
 Butler, F. O., 66
 Buxton, C. L., 100

 Caldwell, R. K., 497
 Calkins, L. A., 549
 Calvert, W., 506
 Camello, A. A., 577
 Campbell, W. R., 676
 Cantarow, A., 246
 Carter, B., 574
 Caton, W. L., 471
 Cattell, R. B., 880

- Hultquist, G., 205
 Humphrey, M. J., 780
 Hundley, J. M., 94, 723, 873
 Hunt, H. B., 124
 Hunter, A. L., 222, 422
 Hunter, F. T., 826
 Hurxthal, L. M., 686
 Igna, E. J., 159
 Ingelman-Sundberg, A., 259, 428
 Ingraham, N. R., 57
 Ingraham, N. R., Jr., 490
 Irwin, J. K. L., 391
 Israel, S. L., 586, 689
 Jackson, M. H., 589
 Jacobi, H., 385
 Jacobson, P., 136
 Jacoby, A., 851
 Jailer, J. W., 800
 Jakobowicz, R., 217
 Jang, G., 207
 Jarcho, J., 625, 628
 Javert, C. T., 426, 624
 Jefferiss, D., 305
 Jennett, R. J., 188
 Jetter, W. W., 826
 Joffe, H. H., 277
 Johnson, A. B., 667
 Johnson, H. W., 359
 Jones, G. E. S., 679
 Jost, H., 40
 Joyce, J. B., 383
 Kaiser, I. H., 526
 Kannapel, A. R., 486
 Kao, H. L., 508
 Kaplan, I. I., 448
 Kardash, T., 132, 723
 Karsh, J., 499
 Kazmierski, R. H., 287
 Regel, A. H., 154
 Keil, H., 834
 Kelley, A. J., 30
 Kelso, J. W., 573
 Kennedy, T. J., 881
 Kernodle, J. R., 113, 529, 698
 Kerr, J. M. M., 333
 Kirschbaum, A., 681
 Kirchhoff, H., 647
 Kistner, R. W., 232, 793
 Knight, W. R., III, 291[†]
 Knowlton, A. I., 488, 800
 Kobrinski, S., 369
 Koch, M. L., 562
 Kraus, A. P., 641
 Kraushaar, O. F., 187
 Krieger, V. I., 217
 Kriss, J. P., 50
 Krohn, P. L., 840
 Kron, W., 691
 Kullander, S., 194
 Kurzrok, R., 304
 Lafferty, H. D., 300
 Landesman, R., 230, 888
 Landowne, M., 189
 Langman, L., 546
 Lapid, L. S., 254
 Lascano, G. M., 557
 Lash, A. F., 144
 Lash, J. J., 692
 Laur, W. E., 852
 Lawlor, M. K., 632
 Lawrence, R. F., 505
 Leatham, J. H., 86, 831
 Lee, T. L., 112
 Lennon, G. G., 383
 L'Esperance, E. S., 113
 Lesse, S., 202
 Levin, W. C., 227
 Levy, S., 655
 Li, K., 118
 Lintgen, C., 721
 Lisa, J. R., 691
 Liu, T. H., 848
 Livingstone, R. G., 253
 Lock, F. R., 847
 Loeb, E. N., 488
 Loeb, L., 711
 Logan, M. A., 633
 Long, R. V., 330
 Lovelady, S. B., 56
 Lubin, S., 485, 710
 Lull, C. B., 339
 Lund, C. J., 801
 Lynch, J. E., 394
 Lynch, K. M., Jr., 874
 MacDonald, E. J., 115
 MacDonald, I., 856
 MacFarlane, C., 598
 MacGregor, A. R., 654
 McCain, J. R., 492
 McCall, M. L., 363, 668
 McCarter, J. C., 292
 McClintock, L., 90
 McDermott, J. C., 787

- Feeney, J. K., 669
 Felsen, J., 53
 Ferris, E. B., 362
 Fetterman, G. H., 830
 Finn, W. F., 63
 Fish, J. S., 349
 Flexner, L. B., 175, 176
 Fluhmann, C. F., 135
 Foote, F. W., 118
 Fouché, H. H., 377
 Fournier, J. C. M., 682
 Fowler, R., 577
 Francisco, C., 796
 Frank, I. L., 564
 Frankel, A. N., 301
 Frantz, M. J., 681
 Fraser, J., 218
 Frazier, E. I., 780
 Fremont-Smith, M., 415
 French, W. G., 703
 Fricke, R. E., 720, 881
 Frymire, L. J., 46
 Fugo, N. W., 99
 Fuller, H. F., 112
 Fulton, L. D., 487
 Furuhielm, M., 403, 404
 Futeher, P. H., 50

 Gandek, C., 643
 Garber, S. T., 793
 Gardner, G. H., 869
 Gastineau, C. F., 29
 Gellis, S. S., 662
 Gemmell, A. A., 299
 Gibson, J. G., 471
 Gilbert, J. A. L., 493
 Gilmore, E. L., 534
 Gluckman, J., 311
 Goff, B. H., 875
 Goldberger, M., 254
 Goldenberg, H., 62
 Goldman, D. W., 443
 Gonzalez, J., 557
 Gordon, C. A., 802
 Gordon, I., 828
 Govan, A. D. T., 489
 Graham, R. M., 123, 415
 Grant, A., 439
 Grant, K. M., 149
 Gray, L. A., 861
 Green, H. S. N., 280
 Greenblatt, R. B., 27, 520, 705, 851
 Greene, B. A., 789
 Greene, R. R., 715, 869

 Greentree, L. B., 687
 Gregory, R., 227
 Griffith, M. L., 847
 Grimes, W. H., Jr., 349
 Gruenwald, P., 65
 Guerriero, W. F., 730
 Guilbeau, J. A., 806
 Gusberg, S. B., 424
 Gustafson, G. W., 387

 Habel, J. M., 404
 Haden, W. D., Jr., 422
 Hadley, J., 199
 Haines, M., 289, 328
 Hall, P. O., 209
 Halpert, B., 565
 Haman, J. O., 441
 Hamilton, J., 556
 Handler, S. H., 57
 Hardie, M., 264
 Harrell, W. B., 550
 Harris, B. A., Jr., 737
 Harris, G. S., 824
 Hart, D., 810
 Hartford, W. K., 565
 Hartl, H., 411
 Harvey, C., 589
 Hawkins, T. F., 631
 Hellman, L. M., 175, 176
 Hendrickson, F. C., 142
 Hendriksen, E., 112
 Hershenson, B. B., 341
 Hertz, R., 701
 Herzig, N., 459
 Hesseltine, H. C., 678
 Heyman, A., 492
 Hickey, B. B., 53
 Hill, L. M., 633
 Hill, R. T., 93
 Hingson, R. A., 350
 Hisaw, F. L., 107
 Hobson, W., 180
 Hoffman, E. S., 797
 Hoge, R. H., 835
 Holzaepfel, J. H., 64
 Horne, E. O., 288
 Howard, P. J., 812
 Howe, J. S., 703
 Howson, J. Y., 547
 Hudgins, A. P., 146
 Huet, J. A., 600
 Huffman, J. W., 704
 Hufford, C. E., 416
 Hughesdon, P. E., 718

- Philpott, N. W., 391
Pierce, L. C., 408
Pierce, V., 702
Pillsbury, S., 483
Platt, L. I., 122
Playfair, P. L., 842
Pollak, O. J., 449
Popenoe, P., 152
Porter, T., 780
Potter, E. L., 87, 650
Potter, M. G., 502
Power, H. A., 204
Power, R. M. H., 155
Prigot, A., 633
Proctor, N. K., 175, 176
Pund, E. R., 808
Purser, R. W. K., 568

Quinlan, D. A., 541

Racker, D. C., 257
Rae, I. P. F., 246
Rakoff, A. E., 86, 241, 246, 523, 546
Ramsdell, E. G., 456
Randall, L. M., 29, 538
Ratner, M., 140
Ravid, J. M., 109
Read, C. O., 575
Reddington, M., 313
Reddock, J. W., 59
Redman, T. F., 279
Reed, H. L., 312
Reel, P. J., 427
Reich, W. J., 533, 850
Reid, D. E., 471, 646
Reis, R. A., 110
Reitman, H., 54
Reycraft, J. L., 883
Reynolds, R. A., 298
Reynolds, S. R. M., 710, 814
Rhaney, K., 654
Ribeiro, P. B., 582
Ricci, J. V., 691
Rice, G. G., 737
Ridley, B., 452
Ries, R. G., 293
Riley, C. L., 497
Riley, G. M., 120
Roberts, J. M., 346
Roby, C. C., 471
Rocha, A. H., 530
Rock, J., 774
Rodrigues, F. V., 583
Rohn, R. J., 643

Roman, D. A., 72
Rommer, J. J., 443
Rose, E. K., 57
Rosenberg, B., 638
Rosenbluth, M. B., 638
Rosenfeld, S. S., 139
Rosenthal, A. E., 638
Rosenthal, A. H., 802
Rosenthal, T., 851
Ross, R. A., 252, 454
Roth, D. B., 445
Rouchy, M. K., 552
Rozin, S., 95, 832
Rubin, I. C., 729
Ruby, B., 189
Rudge, W. de S., 597
Rushforth, W., 733
Russell, B., 223
Russell, S., 295
Rutledge, F., 127
Rydberg, E., 518, 536
Rykert, H. E., 672

Sadugor, M. G., 502
Safford, H. B., 250
St. John, B. D., 717
Sampson, J. J., 794
Sanders, M., 633
Sarrelangue, L. P., 562
Saunders, C., 219
Sayhoun, P., 544
Sayre, G. P., 693
Scharenberg, K., 120
Schaub, I. G., 806
Schaupp, K. L., Jr., 855
Scheffey, L. C., 546
Schneiderman, C., 140
Schott, A., 195
Schumaker, L. B., 142
Scott, J. M., 489
Searle, W. N., 289
Sedgwick, C. E., 882
Seegal, B. C., 488
Seibels, R. E., 399, 414
Sen, N. C., 846
Senra, A., 542
Sewall, C. W., 97
Shands, R. E., 883
Sharman, A., 592
Shaw, W. F., 210
Sheehan, H. L., 804
Shenk, E. P., 343
Shettles, L. B., 614
Shotton, D. M., 503

- McDonough, J. J., 435
 McElin, T. W., 56
 McGanity, W. J., 639
 McGavack, T. H., 84
 McGinn, E. J., 722
 McGoogan, L. S., 124
 McGraw, J., 123
 McGuff, P. E., 538
 McHenry, E. W., 639
 McIntyre, J. P., 47, 375
 McKay, D. G., 121
 McKee, R. D., 805
 McLane, C. M., 36, 584, 692
 McMillan, J. T., 720
 McSweeney, D. J., 121
 Maas, J. M., 130
 Mack, H. C., 860
 Mackey, R., 439
 Magney, F. H., 857
 Maliphaunt, R. G., 423
 Malpas, P., 879
 Manning, J. J., 790
 Marrian, G. F., 781
 Martin, J. P., 107
 Mason, L. M., 410
 Massie, M., 544
 Masters, W. H., 33
 Mathews, R. A., 599
 Mathiesen, K. M., 518
 Mathieu, J., 567
 Mauzy, C. H., 634
 Maxwell, J. P., 854
 Mayer, H. H., 455
 Mayes, B. T., 393
 Mazer, C., 447
 Medina, J., 601
 Meigs, J. V., 272, 415, 878
 Mellow, J., 84
 Mengert, W. F., 188, 315, 335
 Menk, K. F., 716
 Meyerhardt, M. H., 644
 Miller, N. F., 120, 156
 Mills, W. G., 366
 Mino, R. A., 253
 Mino, V. A., 253
 Mohler, R. W., 531, 870
 Mollison, P. L., 653
 Monteiro, A., 555
 Montgomery, T. L., 343
 Moody, J. D., 810
 Moore, C. R., 85
 Morgan, J., 382
 Morgans, M. E., 374, 495
 Morton, J. H., 245
 Moss, J. M., 716
 Mowbray, R., 201, 372
 Mudge, G. H., 800
 Mueller, P. F., 197
 Munnell, E. W., 420
 Murphy, D. P., 450
 Murray, P. M., 725
 Mustard, W. T., 218
 Myller, E., 729
 Nagyfy, S. F., 814
 Nalle, B. C., Jr., 874
 Nathanson, I. T., 878
 Nechtow, M. G., 533, 850
 Newton, B. L., 280
 Nieburgs, H. E., 27
 Nielsen, J. M., 66
 Nixon, J. W., 425
 Nogués, A. E., 521
 Novak, E., 127, 192
 Novak, E. R., 137
 Obermer, E., 178
 O'Brien, W. R., 599
 O'Connor, K. A., 866
 Odenthal, G., 783
 Okie, M. V., 844
 Oliver, E. B., 671
 Oliver, H. M., 288
 Osborn, S. B., 476
 Overstreet, E. W., 307
 Owens, E. U., 656
 Owens, W. C., 656
 Pacheco, U. M., 527
 Page, E. W., 487
 Palmer, A., 1
 Papanicolaou, G. N., 697
 Park, W. W., 540
 Parker, R. T., 574
 Parrett, V., 120
 Parsons, L., 878
 Paschkis, J. E., 246
 Patch, F. S., 141
 Paxson, N. F., 389
 Peckham, B. M., 869
 Pedvis, S., 391
 Peightal, T. C., 131
 Perlin, I. A., 695
 Perlow, S., 641
 Perry, H. A., 655
 Perry, S. P., 422
 Perry, T., 134
 Pfeiffer, C. A., 684

Witschi, E., 91
Wittenberg, S. S., 293
Wolarsky, W., 53
Wolff, W. A., 330
Wood, P. M., 823
Word, B., 559, 671
Wright, H. P., 476
Wright, L. T., 633
Wurstner, T., 473
Wyatt, J., 596
Wyatt, J. P., 62
Wyatt, O. S., 867

Yin, J. C., 848
Yin, M. L., 848
Ylppö, A., 212
Young, J., 568
Yow, M. D., 847
Yudkin, S., 662
Yue, H. S., 120

Zander, E. L., 274
Zeman, F. D., 143
Zondek, B., 95, 240, 832

- Siddall, R. S., 532, 860
Siegler, S. L., 437
Silberblatt, W. B., 250
Simmons, F. A., 446
Simmons, J. M., Jr., 371, 664
Simmons, R. T., 217
Simpson, K., 398
Singer, K., 641
Skinner, I. C., 887
Sloan, W. R., 58
Slovin, T., 250
Small, C., 120
Smith, O. W., 190
Snaith, L., 452
Sobel, N., 851
Solomons, B., 306
Solth, K., 500
Somers, W. H., 44
Sommerville, I. F., 781
Speert, H., 131, 700
Speiser, M. D., 554
Spencer, J. A., 427
Stallworthy, J., 303
Stein, J. J., 406
Stern, K., 215
Stevenson, C. S., 792
Steward, R. E., 343
Stewart, J. J., 852
Still, R. J., 508
Stillman, N., 660
Stoerk, H. C., 488
Stokes, A. B., 675
Stokes, J. H., 57
Stoll, W., 209
Stout, C., 847
Strassmann, E. O., 579
Sturgis, S. H., 123
Suran, R. R., 520, 705
Sutherland, A. M., 535
Sutherland, B. M., 573
Suzuki, M., 797
Sweatt, L. A., 886
Swenson, P. C., 337
Switzer, P. K., 377
Szello, F., 845

Tauber, R., 709
Taylor, A. G., 346
Taylor, C. W., 503
Taylor, E. S., 371
Taylor, H. C., 593
Teilum, G., 864
TeLinde, R. W., 679
Tennent, R. A., 540

Terló, L., 550
Thom, C. H., Jr., 691
Thomas, G. B., 255
Thomas, W. L., 113, 574, 698
Thompson, J. W., 791
Thompson, W., 189
Thomson, G. R., 410
Tietze, C., 221
Torpin, R., 478, 481
Tottenham, R. E., 723
Trapl, J., 296
Trapp, E., 264
Turner, H. B., 350
Twombly, G. H., 90

Ulfelder, H., 119
Underwood, F. J., 397

Van Campenhout, E., 91
Vann, F. H., 44
Van Wyck, H. B., 639, 674
Villaverde, M., 243
Vogel, M., 84
Volpitto, P. P., 481
Vosburgh, G. J., 175, 176

Wallau, F., 379
Walter, R. I., 254, 888
Waltman, R., 485
Wammock, V. S., 57, 851
Watson, J. R., 830
Watt, G. L., 639
Waugh, J. M., 538
Way, S., 558, 566
Weidenbusch, A., 649
Weir, W. C., 572
Wells, A. H., 277
Wells, S. M., 378
Welsh, A. L., 410
West, R. M., 851
Whitacre, F. E., 350
Whitehead, J. P. S., 854
Whitelaw, M. J., 438
Wichern, W. A., 425
Wiener, A. S., 818
Wiener, W. B., 858
Wiesner, B. P., 588
Wilde, W. S., 175, 176
Wilkins, L., 88
Williams, M. F., 401
Williams, W. W., 440
Willson, J. R., 365
Winn, L., 120
Winship, T., 122

- Witschi, E., 91
Wittenberg, S. S., 293
Wolarsky, W., 53
Wolff, W. A., 330
Wood, P. M., 823
Word, B., 559, 671
Wright, H. P., 476
Wright, L. T., 633
Wurstner, T., 473
Wyatt, J., 596
Wyatt, J. P., 62
Wyatt, O. S., 867
Yin, J. C., 848
Yin, M. L., 848
Ylppö, A., 212
Young, J., 568
Yow, M. D., 847
Yudkin, S., 662
Yue, H. S., 120
Zander, E. L., 274
Zeman, F. D., 143
Zondek, B., 95, 240, 832